TherapheresisSeq Listing.txt SEQUENCE LISTING

```
<110> Universitaet Stuttgart
     PFIZENMAIER, Klaus
     SCHEURICH, Peter
     GRUNWALD, Ingo
     KRIPPNER-HEIDENREICH, Anja
<120> RECOMBINANT POLYPEPTIDES OF THE MEMBERS OF THE TNF LIGAND FAMILY AND USE
THEREOF
<130> 040045-0358701
<140> 10/594.189
<141> 2006-09-25
<150> PCT/EP2005/003158
<151> 2005-03-24
<150> DE 102004014983.6-4
<151> 2004-03-26
<160> 41
<170>
      PatentIn version 3.3
<210>
<211>
      8
<212>
      PRT
<213> Artificial Sequence Sequence
<220>
<223> Description of Artificial Sequence: Synthetic flag-tag peptide sequence
<400> 1
ASP Tyr Lys ASP ASP ASP Lys
<210>
      2
<211> 12
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Peptide linker sequence
<400> 2
Gly Gly Gly Ser Gly Gly Ser Gly Gly Gly Ser
<210>
<211>
      16
<212> PRT
<213> Artificial Sequence
<220>
<223>
      Description of Artificial Sequence: Peptide linker sequence
<400>
      3
```

| Gly Gl 1 | y Gly Ser Gly Gly Gly Ser Gly Gly Ser Gly Gly Ser 5 10 15 | |
|----------------------------------|--|----|
| <210> <211> <212> <213> | 4 36 DNA Artificial Sequence | |
| <220> <223> | Description of Artificial Sequence: Linker sequence | |
| <400> ggtggc | 4 ggtt ctggtggcgg ttctggtggc ggatcc | 36 |
| <210> <211> <212> <213> | 5 48 DNA Artificial Sequence | |
| <220> <223> | Description of Artificial Sequence: Linker sequence | |
| <400> ggtggc | 5 ggtt ctggtggcgg ttctggtggc ggttctggtg gcggatcc | 48 |
| <210> <211> <212> <213> | 6 84 DNA Artificial Sequence | |
| <220> <223> | Description of Artificial Sequence: scTNF Primer I | |
| <400> tcgatt | 6 aagc ttcccggggg atccgccacc agaaccgcca ccagaaccgc cacccagagc | 60 |
| gatgat | accg aagtaaacct gacc | 84 |
| <210> <211> <212> <213> | 7 97 DNA Artificial Sequence | |
| <220> <223> | Description of Artificial Sequence: scTNF Primer II | |
| <400> atcgat | 7 taag cttcccgggg gatccgccac cagaaccgcc accagaaccg ccaccagaac | 60 |
| cgccac | ccag agcgatgata ccgaagtaaa cctgacc | 97 |
| <210> <211> <212> <213> | 8 43 DNA Artificial Sequence | |
| <220> | | |

TherapheresisSeg Listing.txt <223> Description of Artificial Sequence: scTNF Primer III <400> 8 ccccgaattc ggatcctctt ctcgtacccc gtctgacaaa ccg 43 <210> 9 <211> 53 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: scTNF Primer IV <400> 9 gggggggaag cttatcgata gttagatatc atcacagagc gatgataccg aag 53 <210> 10 <211> 41 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: scTNF Primer V <400> 10 cctgtacctg atctactccc aggttctgtt caaaggccag g 41 <210> 11 <211> 97 <212> DNA <213> Artificial Sequence <223> Description of Artificial Sequence: cys-scTNF Primer VI <400> 11 aattcattaa agaggagaaa ttaactatgg gagagctcat cgaaggtcgc tgcgccggtg 60 gatctggtca tcatcatcac catcacggct cagacgg 97 <210> 12 <211> 97 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: cys-scTNF Primer VII cgctccgtct gagccgtgat ggtgatgatg atgaccagat ccaccggcgc agcgaccttc 60 gatgagctct cccatagtta atttctcctc tttaatg 97 <210> 13 <211> 100 <212> DNA <213> Artificial Sequence

TherapheresisSeq Listing.txt <220> <223> Description of Artificial Sequence: Primer Fast#1R atcgatttct agacccgggg gatccgccac cagaaccgcc accagaaccg ccaccagaac 60 cgccaccgag cttatataag ccgaaaaacg tctgagattc 100 <210> 14 <211> 35 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: Primer Fast#2F <400> 14 35 ggggtagcgg ccgcgctgtc gacgattaca aagac <210> 15 <211> 26 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: Primer FasL#3F <400> 15 agaaaaaaag gagctgagga aagtgg 26 <210> 16 <211> 36 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: Primer Fast#4F <400> 16 ggggcggatc cgaaaaaaag gagctgagga aagtgg 36 <210> 17 <211> 50 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: Primer FasL#5R <400> 17 ggggcctcta gaatcgatgg tcagagctta tataagccga aaaacgtctg 50 <210> 18 <211> 51 <212> DNA

<220>

<213> Artificial Sequence

TherapheresisSeg Listing.txt <223> Description of Artificial Sequence: Primer HA-IF <400> 18 cgccatggct atcatctacc tcatcctcct gttcaccgct gtgcggggag c 51 <210> 19 <211> 60 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: Primer HA-IIR <400> 19 ggccgctgcc ccgcacagcg gtgaacagga ggatgaggta gatgatagcc atggcggtac 60 <210> 20 <211> 106 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: Primer TRAIL#1R <400> 20 atcgatttct agacccgggg gatccgccac cagaaccgcc accagaaccg ccaccagaac 60 cgccaccgcc aactaaaaag gccccgaaaa aactggcttc atggtc 106 <210> 21 <211> 46 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: Primer TRAIL#2F <400> 21 ggggtagaat tcggaacctc tgaggaaacc atttctacag ttcaag 46 <210> 22 <211> 26 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: Primer TRAIL#3F <400> 22 aacctctgag gaaaccattt ctacag 26 <210> 23 <211> 36 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: Primer TRAIL#4F Page 5

| <400 gggg | | 23 atc | cacci | tctga | ag ga | aaac | catt | t ct | acag | | | | | | | 36 |
|------------------------------|------------------|---------------------------|-------------------|------------------|------------------|--------------------|-------------------|--------------------|------------------|------------------|------------------|-------------------|------------------|------------------|--------------------|-----|
| <210 <211 <212 <213 | > > | 24 53 DNA Arti | ficia | al Se | eque | nce | | | | | | | | | | |
| <220 <223 | | Desci | ript | ion (| of A | rtif | icia | l Se | quen | ce: | Prim | er TI | RAIL | #5R | | |
| <400 gggg | | 24 cta (| gaat | cgat | gg to | cagc | caac | t aa | aaag | gccc | cga | aaaa | act (| ggc | | 53 |
| <210 <211 <212 <213 | L> 2> | 25 1506 DNA Arti | ficia | al Se | equei | ıce | | | | | | | | | | |
| <220 <223 | | Desci | ript [.] | ion (| of Ai | rtif | icia ⁻ | l Se | quen | ce: | scTN | F-L s | shor | t ch | ain | |
| <220 <221 <222 | L> - | CDS (1). | . (150 |)3) | | | | | | | | | | | | |
| | aga | 25 gga Gly | | | | | | | | | | | | | | 48 |
| tct Ser | cgt Arg | acc Thr | ccg Pro 20 | tct Ser | gac Asp | aaa Lys | ccg Pro | gtt val 25 | gct Ala | cac His | gtt Val | gtt Val | gca Ala 30 | aac Asn | ccg Pro | 96 |
| cag Gln | gct Ala | gaa Glu 35 | ggt Gly | caa Gln | ctg Leu | caa Gln | tgg Trp 40 | ctg L eu | aac Asn | cgt Arg | cgt Arg | gct Ala 45 | aac Asn | gct Ala | ctg L eu | 144 |
| ctg L eu | gct Ala 50 | aac Asn | ggt Gly | gtt Val | gaa Glu | ctg Leu 55 | cgt Arg | gac Asp | aac Asn | cag Gln | ctg Leu 60 | gtt Val | gtt Val | ccg Pro | tct Ser | 192 |
| ga a Glu 65 | ggc Gly | ctg L eu | tac Tyr | ctg Leu | atc Ile 70 | tac Tyr | tcc Ser | cag Gln | gtt Val | ctg Leu 75 | ttc Phe | aaa Lys | ggc Gly | cag Gln | ggc Gly 80 | 240 |
| tgc Cys | ccg Pro | tcc Ser | acc Thr | cac His 85 | gtt Val | ctg L eu | ctg Leu | acc Thr | cac His 90 | acc Thr | atc Ile | tct Ser | cgt Arg | atc Ile 95 | gct Ala | 288 |
| | | tac Tyr | | | | | | | | | | | | | | 336 |
| tgc Cys | cag Gln | cgt Arg 115 | gaa Glu | acc Thr | ccg Pro | gaa Glu | ggt Gly 120 | gct Ala | gaa Glu | gct Ala | aaa Lys | ccg Pro 125 | tgg Trp | tac Tyr | gaa Glu | 384 |

| Therapheresisseq Listing.txt ccg atc tac ctg ggt ggc gtt ttt caa ctg gag aaa ggt gac cgt ctg Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Lys Gly Asp Arg Leu 130 135 140 | 432 |
|---|------|
| tct gca gaa att aac cgt ccg gac tac ctg gac ttc gca gaa tct ggt Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe Ala Glu Ser Gly 145 150 150 150 | 480 |
| cag gtt tac ttc ggt atc atc gct ctg ggt ggc ggt tct ggt ggc ggt Gin Val Tyr Phe Gly Ile Ile Ala Leu Gly Gly Gly Ser Gly Gly Gly 175 175 | 528 |
| tct ggt ggc gga tcc tct tct cgt acc ccg tct gac aaa ccg gtt gct Ser Gly Gly Ser Ser Ser Arg Thr Pro Ser Asp Lys Pro Val Ala 185 190 | 576 |
| cac gtt gtt gca aac ccg cag gct gaa ggt caa ctg caa tgg ctg aac His Val Val Ala Asn Pro Gln Ala Glu Gly Gln Leu Gln Trp Leu Asn 195 200 205 | 624 |
| cgt cgt gct aac gct ctg ctg gct aac ggt gtt gaa ctg cgt gac aac Arg Arg Ala Asn Ala Leu Leu Ala Asn Gly Val 2 Glu Leu Arg Asp Asn 2 215 | 672 |
| cag ctg gtt gtt ccg tct gaa ggc ctg tac ctg atc tac tcc cag gtt Gln Leu Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val 225 | 720 |
| ctg ttc aaa ggc cag ggc tgc ccg tcc acc cac gtt ctg ctg acc cac Leu Phe Lys Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu Thr His 245 $$ 255 $$ | 768 |
| acc atc tct cgt atc gct gtt tcc tac cag acc aaa gta aac ctg ctg Thr Ile Ser Arg Ile Ala Val Ser Tyr Gln Thr Lys Val Asn Leu Leu 260 Asn Leu Leu 270 | 816 |
| tct gca atc aaa tct ccg tgc cag cgt gaa acc ccg gaa ggt gct gaa Ser Ala Ile Lys Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu 275 285 285 | 864 |
| gct aaa ccg tgg tac gaa ccg atc tac ctg ggt ggc gtt ttt caa ctg Ala Lys Pro Trp Tyr Glu Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu 290 $$ | 912 |
| gag aaa ggt gac cgt ctg tct gca gaa att aac cgt ccg gac tac ctg Glu Lys Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu 305 $$ 310 $$ 310 $$ 315 | 960 |
| gac ttc gca gaa tct ggt cag gtt tac ttc ggt atc atc gct ctg ggt Asp Phe Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala Leu Gly $^{325}_{225}$ | 1008 |
| ggc ggt tct ggt ggc ggt tct ggt ggc gga tcc tct tct cgt acc ccg Gly Gly Ser Gly Gly Ser Ser Ser Arg Thr Pro 340 | 1056 |
| tct gac aaa ccg gtt gct cac gtt gtt gca aac ccg cag gct gaa ggt Ser Asp Lys Pro Val Ala His Val Val Ala Asn Pro Gln Ala Glu Gly 355 360 365 | 1104 |
| caa ctg caa tgg ctg aac cgt cgt gct aac gct ctg ctg gct aac ggt Gln Leu Gln Trp Leu Asn Arg Arg Ala Asn Ala Leu Leu Ala Asn Gly 370 | 1152 |

280 Page 7

| gtt gaa ctg c Val Glu Leu A 385 | gt gac aac cag arg Asp Asn Gln 390 | Leu Val Val | ccg tct gaa ggc Pro Ser Glu Gly 395 | ctg tac 1200 Leu Tyr 400 |
|---|--|-----------------------------------|---|--------------------------------|
| ctg atc tac t Leu Ile Tyr S | cc cag gtt ctg ser Gln Val Leu 405 | ttc aaa ggc Phe Lys Gly 410 | cag ggc tgc ccg Gln Gly Cys Pro | tcc acc 1248 Ser Thr 415 |
| His Val Leu L | tg acc cac acc eu Thr His Thr 20 | atc tct cgt Ile Ser Arg 425 | atc gct gtt tcc Ile Ala Val Ser 430 | tac cag 1296 Tyr Gln |
| | | | tct ccg tgc cag Ser Pro Cys Gln 445 | |
| acc ccg gaa g Thr Pro Glu G 450 | gt gct gaa gct ily Ala Glu Ala 455 | aaa ccg tgg Lys Pro Trp | tac gaa ccg atc Tyr Glu Pro Ile 460 | tac ctg 1392 Tyr Leu |
| ggt ggc gtt t Gly Gly Val P 465 | tt caa ctg gag he Gln Leu Glu 470 | Lys Gly Asp | cgt ctg tct gca Arg Leu Ser Ala 475 | gaa att 1440 Glu Ile 480 |
| aac cgt ccg g Asn Arg Pro A | ac tac ctg gac sp Tyr Leu Asp 485 | ttc gca gaa Phe Ala Glu 490 | tct ggt cag gtt Ser Gly Gln Val | tac ttc 1488 Tyr Phe 495 |
| ggt atc atc g Gly Ile Ile A 5 | | | | 1506 |
| <210> 26 <211> 501 <212> PRT <213> Artific | cial Sequence | | | |
| <220> <223> Descri | ption of Artif | icial Sequenc | e: scTNF-L short | chain peptide |
| <400> 26 | | | | |
| Met Arg Gly So 1 | er His His His 5 | ніs ніs ніs d 10 | Gly Ser Ala Ser | Ser Ser 15 |
| Ser Arg Thr P | | Pro Val Ala 1 25 | His Val Val Ala A 30 | Asn Pro |
| Gln Ala Glu G | ly Gln Leu Gln | Trp Leu Asn 4 | Arg Arg Ala Asn / 45 | Ala Leu |

Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu Val Val Pro Ser $50 \hspace{1.5cm} 60$

Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile Ser Arg Ile Ala 85 90 95 Val Ser Tyr Gln Thr Lys Val Asn Leu Leu Ser Ala Ile Lys Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Lys Pro Trp Tyr Glu 115 120 125 Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Lys Gly Asp Arg Leu 130 135 140 Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe Ala Glu Ser Gly 145 155 160 Gln Val Tyr Phe Gly Ile Ile Ala Leu Gly Gly Gly Ser Gly Gly Gly 175 Ser Gly Gly Ser Ser Ser Arg Thr Pro Ser Asp Lys Pro Val Ala 180 185 190 His Val Val Ala Asn Pro Gln Ala Glu Gly Gln Leu Gln Trp Leu Asn 195 200 205 Arg Arg Ala Asn Ala Leu Leu Ala Asn Gly Val Glu Leu Arg Asp Asn 210 220 Gln Leu Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val 225 230 235 240 Leu Phe Lys Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu Thr His 245 250 255 Thr Ile Ser Arg Ile Ala Val Ser Tyr Gln Thr Lys Val Asn Leu Leu 260 265 270 Ser Ala Ile Lys Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu 275 280 285 Ala Lys Pro Trp Tyr Glu Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu 290 295 300 Glu Lys Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu 305 310 315 320Asp Phe Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala Leu Gly 325 330 335

Gly Gly Ser Gly Gly Gly Ser Gly Gly Ser Ser Ser Arg Thr Pro 340 345 350 Ser Asp Lys Pro Val Ala His Val Val Ala Asn Pro Gln Ala Glu Gly 355 360 365 Gln Leu Gln Trp Leu Asn Arg Arg Ala Asn Ala Leu Leu Ala Asn Gly 370 375 380 Val Glu Leu Arg Asp Asn Gln Leu Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu Phe Lys Gly Gln Gly Cys Pro Ser Thr 405 410 415His Val Leu Ceu Thr His Thr Ile Ser Arg Ile Ala Val Ser Tyr Gln
420 425 430 Thr Lys Val Asn Leu Leu Ser Ala Ile Lys Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Lys Pro Trp Tyr Glu Pro Ile Tyr Leu 450 455 460 Gly Gly Val Phe Gln Leu Glu Lys Gly Asp Arg Leu Ser Ala Glu Ile 465 470 475 480 Asn Arg Pro Asp Tyr Leu Asp Phe Ala Glu Ser Gly Gln Val Tyr Phe 485 490 495 Gly Ile Ile Ala Leu <210> 27 1542 <211> <212> DNA Artificial Sequence <220> <223> Description of Artificial Sequence: cys-scTNF-L short chain

<220> <221> CDS <222> (1)..(1539)

| | | | | | | | | | | | | | . | - | | |
|-------------------|-------------------|-------------------|-------------------|---------------------|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|-------------------|-------------------|--------------------|-----|
| cat His | cac His | cat His | cac His 20 | ggc Gly | tca S er | gac Asp | gga Gly | gcg Ala 25 | tcg Ser | tct Ser | tct Ser | tct S er | cgt Arg 30 | acc Thr | ccg P ro | 96 |
| tct Ser | gac Asp | aaa Lys 35 | ccg Pro | gtt Val | gct Ala | cac His | gtt val 40 | gtt Val | gca Ala | aac Asn | ccg Pro | cag Gln 45 | gct Ala | gaa Glu | ggt Gly | 144 |
| caa Gln | ctg Leu 50 | caa Gln | tgg Trp | ctg L e u | aac Asn | cgt Arg 55 | cgt Arg | gct Ala | aac Asn | gct Ala | ctg Leu 60 | ctg Leu | gct Ala | aac Asn | ggt Gly | 192 |
| gtt Va1 65 | gaa Glu | ctg Leu | cgt Arg | gac Asp | aac Asn 70 | cag Gln | ctg Leu | gtt Val | gtt val | ccg Pro 75 | tct Ser | gaa Glu | ggc Gly | ctg Leu | tac Tyr 80 | 240 |
| ctg Leu | atc Ile | tac Tyr | tcc Ser | cag G1n 85 | gtt val | ctg Leu | ttc Phe | aaa Lys | ggc G1y 90 | cag Gln | ggc Gly | tgc Cys | ccg Pro | tcc ser 95 | acc Thr | 288 |
| | | | | | | acc Thr | | | | | | | | | | 336 |
| acc Thr | aaa Lys | gta val 115 | aac Asn | ctg Leu | ctg Leu | tct Ser | gca Ala 120 | atc Ile | aaa Lys | tct Ser | ccg Pro | tgc Cys 125 | cag Gln | cgt Arg | gaa Glu | 384 |
| acc Thr | ccg Pro 130 | gaa Glu | ggt Gly | gct Ala | gaa Glu | gct Ala 135 | aaa Lys | ccg Pro | tgg Trp | tac Tyr | gaa Glu 140 | ccg Pro | atc Ile | tac Tyr | ctg Leu | 432 |
| ggt Gly 145 | ggc Gly | gtt val | ttt Phe | caa Gln | ctg Leu 150 | gag Glu | aaa Lys | ggt Gly | gac Asp | cgt Arg 155 | ctg Leu | tct Ser | gca Ala | gaa Glu | att Ile 160 | 480 |
| aac Asn | cgt Arg | ccg Pro | gac Asp | tac Tyr 165 | ctg Leu | gac Asp | ttc Phe | gca Ala | gaa Glu 170 | tct Ser | ggt Gly | cag Gln | gtt val | tac Tyr 175 | ttc Phe | 528 |
| ggt Gly | atc Ile | atc Ile | gct Ala 180 | ctg Leu | ggt Gly | ggc Gly | ggt Gly | tct Ser 185 | ggt Gly | ggc Gly | ggt Gly | tct Ser | ggt Gly 190 | ggc Gly | gga Gly | 576 |
| tcc Ser | tct Ser | tct Ser 195 | cgt Arg | acc Thr | ccg Pro | tct Ser | gac Asp 200 | aaa Lys | ccg Pro | gtt Val | gct Ala | cac His 205 | gtt Val | gtt Val | gca Ala | 624 |
| aac Asn | ccg Pro 210 | cag Gln | gct Ala | gaa Glu | ggt Gly | caa Gln 215 | ctg Leu | caa Gln | tgg Trp | ctg Leu | aac Asn 220 | cgt Arg | cgt Arg | gct Ala | aac Asn | 672 |
| gct Ala 225 | ctg Leu | ctg Leu | gct Ala | aac Asn | ggt Gly 230 | gtt Val | gaa Glu | ctg Leu | cgt Arg | gac Asp 235 | aac Asn | cag Gln | ctg Leu | gtt Val | gtt Val 240 | 720 |
| | | | | | | ctg Leu | | | | | | | | | | 768 |
| cag Gln | ggc Gly | tgc Cys | ccg Pro | tcc Ser | acc Thr | cac His | gtt Val | ctg Leu | Leu | acc Thr age | His | acc Thr | atc Ile | tct Ser | cgt Arg | 816 |

| atc Ile | gct Ala | gtt Val 275 | tcc Ser | tac Tyr | cag Gln | acc Thr | aaa Lys 280 | gta Val | aac Asn | ctg Leu | ctg Leu | tct Ser 285 | gca Ala | atc Ile | aaa Lys | 864 |
|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| tct Ser | ccg Pro 290 | tgc Cys | cag Gln | cgt Arg | gaa Glu | acc Thr 295 | ccg Pro | gaa Glu | ggt Gly | gct Ala | gaa Glu 300 | gct Ala | aaa Lys | ccg Pro | tgg Trp | 912 |
| tac Tyr 305 | gaa Glu | ccg Pro | atc Ile | tac Tyr | ctg Leu 310 | ggt Gly | ggc GTy | gtt Val | ttt Phe | caa Gln 315 | ctg Leu | gag Glu | aaa Lys | ggt Gly | gac Asp 320 | 960 |
| cgt Arg | ctg Leu | tct Ser | gca Ala | gaa Glu 325 | att Ile | aac Asn | cgt Arg | ccg Pro | gac Asp 330 | tac Tyr | ctg Leu | gac Asp | ttc Phe | gca Ala 335 | gaa Glu | 1008 |
| tct Ser | ggt Gly | cag Gln | gtt Val 340 | tac Tyr | ttc Phe | ggt Gly | atc Ile | atc Ile 345 | gct Ala | ctg Leu | ggt Gly | ggc Gly | ggt Gly 350 | tct Ser | ggt Gly | 1056 |
| ggc G1y | ggt Gly | tct ser 355 | ggt Gly | ggc Gly | gga Gly | tcc Ser | tct Ser 360 | tct Ser | cgt Arg | acc Thr | ccg Pro | tct Ser 365 | gac Asp | aaa Lys | ccg Pro | 1104 |
| gtt val | gct Ala 370 | cac His | gtt Val | gtt val | gca Ala | aac Asn 375 | ccg Pro | cag Gln | gct Ala | gaa Glu | ggt Gly 380 | caa Gln | ctg Leu | caa Gln | tgg Trp | 1152 |
| ctg Leu 385 | aac Asn | cgt Arg | cgt Arg | gct Ala | aac Asn 390 | gct Ala | ctg Leu | ctg Leu | gct Ala | aac Asn 395 | ggt Gly | gtt Val | gaa Glu | ctg Leu | cgt Arg 400 | 1200 |
| gac Asp | aac Asn | cag Gln | ctg Leu | gtt val 405 | gtt Val | ccg Pro | tct Ser | gaa Glu | ggc Gly 410 | ctg Leu | tac Tyr | ctg Leu | atc Ile | tac Tyr 415 | tcc Ser | 1248 |
| cag Gln | gtt Val | ctg Leu | ttc Phe 420 | aaa Lys | ggc Gly | cag Gln | ggc Gly | tgc Cys 425 | ccg Pro | tcc Ser | acc Thr | cac His | gtt Val 430 | ctg Leu | ctg Leu | 1296 |
| acc Thr | cac His | acc Thr 435 | atc Ile | tct Ser | cgt Arg | atc Ile | gct Ala 440 | gtt Val | tcc Ser | tac Tyr | cag Gln | acc Thr 445 | aaa Lys | gta Val | aac Asn | 1344 |
| ctg L eu | ctg Leu 450 | tct Ser | gca Ala | atc Ile | aaa Lys | tct Ser 455 | ccg Pro | tgc Cys | cag Gln | cgt Arg | gaa Glu 460 | acc Thr | ccg Pro | gaa Glu | ggt Gly | 1392 |
| gct Ala 465 | gaa Glu | gct Ala | aaa Lys | ccg Pro | tgg Trp 470 | tac Tyr | gaa Glu | ccg Pro | atc Ile | tac Tyr 475 | ctg Leu | ggt Gly | ggc Gly | gtt Val | ttt Phe 480 | 1440 |
| caa Gln | ctg Leu | gag Glu | aaa Lys | ggt Gly 485 | gac Asp | cgt Arg | ctg Leu | tct Ser | gca Ala 490 | gaa Glu | att Ile | aac Asn | cgt Arg | ccg Pro 495 | gac Asp | 1488 |
| tac Tyr | ctg Leu | gac Asp | ttc Phe 500 | gca Ala | gaa Glu | tct Ser | ggt Gly | cag G1n 505 | gtt Val | tac Tyr | ttc Phe | ggt Gly | atc Ile 510 | atc Ile | gct Ala | 1536 |
| ctg | tga | | | | | | | | Р | age | 12 | | | | | 1542 |

Leu

<210>

28 513 <211> <212> Artificial Sequence <220> Description of Artificial Sequence: cys-scTNF-L short peptide <223> <400> 28 Met Gly Glu Leu Ile Glu Gly Arg Cys Ala Gly Gly Ser Gly His $1 \ \ \, 10 \ \ \, 15$ His His His Gly Ser Asp Gly Ala Ser Ser Ser Arg Thr Pro 20 25 30 Ser Asp Lys Pro Val Ala His Val Val Ala Asn Pro Gln Ala Glu Gly $35 \hspace{1cm} 40 \hspace{1cm} 45$ Gln Leu Gln Trp Leu Asn Arg Arg Ala Asn Ala Leu Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu Val Val Pro Ser Glu Gly Leu Tyr 65 70 75 80 Leu Ile Tyr Ser Gln Val Leu Phe Lys Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile Ser Arg Ile Ala Val Ser Tyr Gln $100 \hspace{1cm} 105$ Thr Lys Val Asn Leu Leu Ser Ala Ile Lys Ser Pro Cys Gln Arg Glu 115 120 125 Thr Pro Glu Gly Ala Glu Ala Lys Pro Trp Tyr Glu Pro Ile Tyr Leu 130 135 140 Gly Gly Val Phe Gln Leu Glu Lys Gly Asp Arg Leu Ser Ala Glu Ile 145 150 155 160 Asn Arg Pro Asp Tyr Leu Asp Phe Ala Glu Ser Gly Gln Val Tyr Phe 165 170 175 Gly Ile Ile Ala Leu Gly Gly Gly Ser Gly Gly Gly Gly 180 185 190 Ser Ser Ser Arg Thr Pro Ser Asp Lys Pro Val Ala His Val Val Ala Page 13

Asn Pro Gln Ala Glu Gly Gln Leu Gln Trp Leu Asn Arg Arg Ala Asn 210 215 220 Ala Leu Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu Val Val 225 230 235 240 Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu Phe Lys Gly 245 250 255 Gln Gly Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile Ser Arg 260 265 270 Ile Ala Val Ser Tyr Gln Thr Lys Val Asn Leu Leu Ser Ala Ile Lys 275 280 285 Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Lys Pro Trp 290 295 300Tyr Glu Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Lys Gly Asp 305 310 315 320 Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe Ala Glu 325 330 335 Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala Leu Gly Gly Gly Ser Gly 340 345 350 Gly Gly Ser Gly Gly Gly Ser Ser Ser Arg Thr Pro Ser Asp Lys Pro 355 360 365Val Ala His Val Val Ala Asn Pro Gln Ala Glu Gly Gln Leu Gln Trp 370 375 380 Leu Asn Arg Arg Ala Asn Ala Leu Leu Ala Asn Gly Val Glu Leu Arg 385 390 395 400 Asp Asn Gln Leu Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser 405 410 415 Gln Val Leu Phe Lys Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu 420 425 430 Thr His Thr Ile Ser Arg Ile Ala Val Ser Tyr Gln Thr Lys Val Asn 435 440 445

Leu Leu Ser Ala Ile Lys Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly
450 455 460 Ala Glu Ala Lys Pro Trp Tyr Glu Pro Ile Tyr Leu Gly Gly Val Phe 465 470 475 480 465 Gln Leu Glu Lys Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp 485 490 495 Tyr Leu Asp Phe Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala 500 505 510 Leu <210> 29 1476 <211> <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: scFasL sequence <220> <221> <222> CDS (1)..(1473) atg gct atc atc tac ctc atc ctc ctg ttc acc gct gtg cgg gcg Met Ala Ile Ile Tyr Leu Ile Leu Leu Phe Thr Ala Val Arg Gly Ala 1 48 gcc gcg gat tac aaa gac gat gac gat aaa gaa ttc acg cgt gaa aaa Ala Ala Asp Tyr Lys Asp Asp Asp Lys Glu Phe Thr Arg Glu Lys 20 20 30 96 aag gag ctg agg aaa gtg gcc cat tta aca ggc aag tcc aac tca agg Lys Glu Leu Arg Lys Val Ala His Leu Thr Gly Lys Ser Asn Ser Arg 35 40 144 tcc atg cct ctg gaa tgg gaa gac acc tat gga att gtc ctg ctt tct Ser Met Pro Leu Glu Trp Glu Asp Thr Tyr Gly Ile Val Leu Leu Ser 192 gga gtg aag tat aag aag ggt ggc ctt gtg atc aat gaa act ggg ctg Gly Val Lys Tyr Lys Lys Gly Gly Leu Val Ile Asn Glu Thr Gly Leu 65 70 80 240 288 tac ttt gta tat tcc aaa gta tac ttc cgg ggt caa tct tgc aac aac Tyr Phe Val Tyr Ser Lys Val Tyr Phe Arg Gly Gln Ser Cys Asn Asn ctg ccc ctg agc cac aag gtc tac atg agg aac tct aag tat ccc cag Leu Pro Leu Ser H1s Lys Val Tyr Met Arg Asn Ser Lys Tyr Pro Gln 100 100 10336 gat ctg gtg atg atg gag ggg aag atg atg agc tac tgc act act ggg 384 Page 15

| Asp | Leu | val 115 | Met | Met | Glu | Gly | The Lys 120 | raph Met | eres Met | isse Ser | q Li Tyr | stin Cys 125 | g.tx Thr | t Thr | Gly | |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|-------------------|-------------------|-------------------|------|
| cag Gln | atg Met 130 | tgg Trp | gcc Ala | cgc Arg | agc Ser | agc Ser 135 | tac Tyr | ctg Leu | ggg Gly | gca Ala | gtg Val 140 | ttc Phe | aat Asn | ctt Leu | acc Thr | 432 |
| agt Ser 145 | gct Ala | gat Asp | cat His | tta Leu | tat Tyr 150 | gtc Val | aac Asn | gta Val | tct Ser | gag Glu 155 | ctc Leu | tct Ser | ctg Leu | gtc Val | aat Asn 160 | 480 |
| ttt Phe | gag Glu | gaa Glu | tct Ser | cag Gln 165 | acg Thr | ttt Phe | ttc Phe | ggc Gly | tta Leu 170 | tat Tyr | aag Lys | ctc Leu | ggt Gly | ggc Gly 175 | ggt Gly | 528 |
| tct Ser | ggt Gly | ggc Gly | ggt Gly 180 | tct Ser | ggt Gly | ggc Gly | ggt Gly | tct Ser 185 | ggt Gly | ggc Gly | gga Gly | tca Ser | gaa Glu 190 | aaa Lys | aag Lys | 576 |
| gag Glu | ctg Leu | agg Arg 195 | aaa Lys | gtg Val | gcc Ala | cat His | tta Leu 200 | aca Thr | ggc Gly | aag Lys | tcc Ser | aac Asn 205 | tca Ser | agg Arg | tcc Ser | 624 |
| atg Met | cct Pro 210 | ctg Leu | gaa Glu | tgg Trp | gaa Glu | gac Asp 215 | acc Thr | tat Tyr | gga Gly | att Ile | gtc Val 220 | ctg Leu | ctt Leu | tct Ser | gga Gly | 672 |
| gtg Val 225 | aag Lys | tat Tyr | aag Lys | aag Lys | ggt Gly 230 | ggc Gly | ctt Leu | gtg Va l | atc Ile | aat Asn 235 | gaa Glu | act Thr | ggg Gly | ctg Leu | tac Tyr 240 | 720 |
| ttt Phe | gta Val | tat Tyr | tcc Ser | aaa Lys 245 | gta Val | tac Tyr | ttc Phe | cgg Arg | ggt Gly 250 | caa Gln | tct Ser | tgc Cys | aac Asn | aac Asn 255 | ctg Leu | 768 |
| ccc Pro | ctg Leu | agc Ser | cac His 260 | aag Lys | gtc Val | tac Tyr | atg Met | agg Arg 265 | aac Asn | tct Ser | aag Lys | tat Tyr | ccc Pro 270 | cag Gln | gat Asp | 816 |
| ctg Leu | gtg Val | atg Met 275 | atg Met | gag Glu | ggg Gly | aag Lys | atg Met 280 | atg Met | agc Ser | tac Tyr | tgc Cys | act Thr 285 | act Thr | ggg GTy | cag Gln | 864 |
| atg Met | tgg Trp 290 | gcc Ala | cgc Arg | agc Ser | agc Ser | tac Tyr 295 | ctg Leu | ggg Gly | gca Ala | gtg Va I | ttc Phe 300 | aat Asn | ctt Leu | acc Thr | agt Ser | 912 |
| gct Ala 305 | gat Asp | cat His | tta Leu | tat Tyr | gtc Val 310 | aac Asn | gta Val | tct Ser | gag Glu | ctc Leu 315 | tct Ser | ctg Leu | gtc Val | aat Asn | ttt Phe 320 | 960 |
| gag Glu | gaa Glu | tct Ser | cag Gln | acg Thr 325 | ttt Phe | ttc Phe | ggc Gly | tta Leu | tat Tyr 330 | aag Lys | ctc Leu | ggt Gly | ggc Gly | ggt Gly 335 | tct Ser | 1008 |
| ggt Gly | ggc Gly | ggt Gly | tct Ser 340 | ggt Gly | ggc Gly | ggt Gly | tct Ser | ggt Gly 345 | ggc Gly | gga Gly | tcc Ser | gaa Glu | aaa Lys 350 | aag Lys | gag Glu | 1056 |
| ctg Leu | agg Arg | aaa Lys 355 | gtg Val | gcc Ala | cat His | tta Leu | aca Thr 360 | ggc Gly | aag Lys | tcc Ser | aac Asn | tca Ser 365 | agg Arg | tcc Ser | atg Met | 1104 |

```
TherapheresisSeq Listing.txt
cct ctg gaa tgg gaa gac acc tat gga att gtc ctg ctt tct gga gtg
Pro Leu Glu Trp Glu Asp Thr Tyr Gly Ile Val Leu Leu Ser Gly Val
                                                                                                           1152
aag tat aag aag ggt ggc ctt gtg atc aat gaa act ggg ctg tac ttt
Lys Tyr Lys Lys Gly Gly Leu Val Ile Asn Glu Thr Gly Leu Tyr Phe
385
                                                                                                           1200
gta tat tcc aaa gta tac ttc cgg ggt caa tct tgc aac aac ctg ccc
Val Tyr Ser Lys Val Tyr Phe Arg Gly Gln Ser Cys Asn Asn Leu Pro
                                                                                                           1248
ctg agc cac aag gtc tac atg agg aac tct aag tat ccc cag gat ctg Leu Ser His Lys Val Tyr Met Arg Asn Ser Lys Tyr Pro \overline{G}ln Asp Leu \overline{420} \overline{420}
                                                                                                           1296
gtg atg atg gag ggg aag atg atg agc tac tgc act act ggg cag atg
Val Met Met Glu Gly Lys Met Met Ser Tyr Cys Thr Thr Gly Gln Met
                                                                                                           1344
tgg gcc cgc agc agc tac ctg ggg gca gtg ttc aat ctt acc agt gct
Trp Ala Arg Ser Ser Tyr Leu Gly Ala Val Phe Asn Leu Thr Ser Ala
450 460
                                                                                                           1392
gat cat tta tat gtc aac gta tct gag ctc tct ctg gtc aat ttt gag
Asp His Leu Tyr Val Asn Val Ser Glu Leu Ser Leu Val Asn Phe Glu
465 470
                                                                                                           1440
gaa tct cag acg ttt ttc ggc tta tat aag ctc tga
Glu Ser Gln Thr Phe Phe Gly Leu Tyr Lys Leu
485
486
                                                                                                           1476
<210>
           30
<211>
           491
<212>
           PRT
           Artificial Sequence
<220>
<223> Description of Artificial Sequence: scFasL peptide sequence
Met Ala Ile Ile Tyr Leu Ile Leu Leu Phe Thr Ala Val Arg Gly Ala
Ala Ala Asp Tyr Lys Asp Asp Asp Lys Glu Phe Thr Arg Glu Lys
Lys Glu Leu Arg Lys Val Ala His Leu Thr Gly Lys Ser Asn Ser Arg
Ser Met Pro Leu Glu Trp Glu Asp Thr Tyr Gly Ile Val Leu Leu Ser
Gly Val Lys Tyr Lys Lys Gly Gly Leu Val Ile Asn Glu Thr Gly Leu
```

TherapheresisSeq Listing.txt Tyr Phe Val Tyr Ser Lys Val Tyr Phe Arg Gly Gln Ser Cys Asn Asn 90 95 Leu Pro Leu Ser His Lys Val Tyr Met Arg Asn Ser Lys Tyr Pro Gln
100 105 110 Asp Leu Val Met Met Glu Gly Lys Met Met Ser Tyr Cys Thr Thr Gly Gln Met Trp Ala Arg Ser Ser Tyr Leu Gly Ala Val Phe Asn Leu Thr 130 135 140 Ser Ala Asp His Leu Tyr Val Asn Val Ser Glu Leu Ser Leu Val Asn 145 150 150 155 160 Phe Glu Glu Ser Gln Thr Phe Phe Gly Leu Tyr Lys Leu Gly Gly Gly 175 175 Ser Gly Gly Gly Ser Gly Gly Gly Gly Gly Ser Glu Lys Lys 180 185 190 Glu Leu Arg Lys Val Ala His Leu Thr Gly Lys Ser Asn Ser Arg Ser Met Pro Leu Glu Trp Glu Asp Thr Tyr Gly Ile Val Leu Leu Ser Gly 210 215 220 Val Lys Tyr Lys Lys Gly Gly Leu Val Ile Asn Glu Thr Gly Leu Tyr 225 230 235 240 Phe Val Tyr Ser Lys Val Tyr Phe Arg Gly Gln Ser Cys Asn Asn Leu 245 250 255 Pro Leu Ser His Lys Val Tyr Met Arg Asn Ser Lys Tyr Pro Gln Asp 260 265 270 Leu Val Met Met Glu Gly Lys Met Met Ser Tyr Cys Thr Thr Gly Gln 275 280 285 Met Trp Ala Arg Ser Ser Tyr Leu Gly Ala Val Phe Asn Leu Thr Ser 290 295 300 Ala Asp His Leu Tyr Val Asn Val Ser Glu Leu Ser Leu Val Asn Phe 305 310 315 320 Glu Glu Ser Gln Thr Phe Phe Gly Leu Tyr Lys Leu Gly Gly Gly Ser 325 330 335

| Gly (| Gly | Gly | Ser 340 | Gly | Gly | Gly | Ser | Gly 345 | Gly | Gly | Ser | Glu | Lys 350 | Lys | Glu | |
|----------------------------------|------------|----------------------------|------------------|-----------------|------------|------------|------------|-------------------|------------------|------------|------------|------------|------------------|------------------|------------|-----|
| Leu A | ٩rg | Lys 355 | Val | Αla | His | Leu | Thr 360 | Gly | Lys | Ser | Asn | Ser 365 | Arg | Ser | Met | |
| Pro I | Leu 370 | Glu | Trp | Glu | Asp | Thr 375 | Tyr | G1y | Ile | Val | Leu 380 | Leu | Ser | Gly | Val | |
| Lys ⁻ 385 | Tyr | Lys | Lys | Gly | G1y 390 | Leu | Val | Ile | Asn | G]u 395 | Thr | Gly | Leu | Tyr | Phe 400 | |
| val - | Tyr | Ser | Lys | Val 405 | Tyr | Phe | Arg | Gly | G]n 410 | Ser | Cys | Asn | Asn | Leu 415 | Pro | |
| Leu : | Ser | ніѕ | Lys 420 | ۷al | Tyr | Met | Arg | Asn 425 | Ser | Lys | Tyr | Pro | G1n 430 | Asp | Leu | |
| val 1 | мet | Met 435 | Glu | G] y | Lys | Met | Met 440 | Ser | туг | Cys | Thr | Thr 445 | Gly | Gln | Met | |
| Trp / | 41a 450 | Arg | Ser | Ser | Tyr | Leu 455 | Gly | Аlа | val | Phe | Asn 460 | Leu | Thr | Ser | Ala | |
| Asp 1 465 | нis | Leu | Tyr | val | Asn 470 | ۷al | Ser | Glu | Leu | Ser 475 | Leu | val | Asn | Phe | G]u 480 | |
| Glu : | Ser | Gln | Thr | Phe 485 | Phe | GТу | Leu | Tyr | Lys 490 | Leu | | | | | | |
| <210: <211: <212: <213: | > 1 > [| 81 L869 DNA Artif | ficia | ıl Se | equer | ıce | | | | | | | | | | |
| <220: <223: | | escr | ipti | ion d | of Ar | tifi | icia | l Sec | quenc | :e: s | scTR/ | AIL S | seque | ence | | |
| <220: <221: <222: | > (| DS (1) | (186 | 56) | | | | | | | | | | | | |
| <400: atg Met 1 | gct | atc Ile | atc Ile | tac Tyr 5 | ctc Leu | atc Ile | ctc Leu | ctg Leu | ttc Phe 10 | acc Thr | gct Ala | gtg Val | cgg Arg | ggc Gly 15 | gcg Ala | 48 |
| gcc Ala | gcg Ala | gat Asp | tac Tyr 20 | aaa Lys | gac Asp | gat Asp | gac Asp | gat Asp 25 | aaa Lys | gaa Glu | ttc Phe | gga GTy | acc Thr 30 | tct Ser | gag Glu | 96 |
| gaa | acc | att | tct | aca | gtt | caa | gaa | aag | | caa | | att | tct | ccc | cta | 144 |

| | | | | | | | The | raph | eres | isse | a Li | stin | a.tx | t | | |
|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----|
| Glu | Thr | Ile 35 | Ser | Thr | va1 | Gln | G1u 40 | Lys | Gln | G1n | Asn | 11e 45 | Ser | Pro | Leu | |
| gtg Val | aga Arg 50 | gaa Glu | aga Arg | ggt Gly | cct P ro | cag G1n 55 | aga Arg | gta Val | gca Ala | gct Ala | cac His 60 | ata Ile | act Thr | ggg Gly | acc Thr | 192 |
| aga Arg 65 | gga Gly | aga Arg | agc Ser | aac Asn | aca Thr 70 | ttg Leu | tct Ser | tct Ser | cca Pro | aac Asn 75 | tcc Ser | aag Lys | aat Asn | gaa Glu | aag Lys 80 | 240 |
| gct Ala | ctg Leu | ggc G1y | cgc Arg | aaa Lys 85 | ata Ile | aac Asn | tcc Ser | tgg Trp | gaa G1u 90 | tca Ser | tca Ser | agg Arg | agt Ser | ggg G Ty 95 | cat His | 288 |
| tca Ser | ttc Phe | ctg Leu | agc Ser 100 | aac Asn | ttg Leu | cac His | ttg Leu | agg Arg 105 | aat Asn | ggt Gly | gaa Glu | ctg Leu | gtc Val 110 | atc Ile | cat His | 336 |
| | | | | | tac Tyr | | | | | | | | | | | 384 |
| gag Glu | gaa Glu 130 | ata Ile | aaa Lys | gaa Glu | aac Asn | aca Thr 135 | aag Lys | aac Asn | gac Asp | aaa Lys | caa Gln 140 | atg Met | gtc Val | caa Gln | tat Tyr | 432 |
| att Ile 145 | tac Tyr | aaa Lys | tac Tyr | aca Thr | agt Ser 150 | tat Tyr | cct Pro | gac Asp | cct Pro | ata Ile 155 | ttg Leu | ttg Leu | atg Met | aaa Lys | agt Ser 160 | 480 |
| gct Ala | aga Arg | aat Asn | agt Ser | tgt Cys 165 | tgg Trp | tct Ser | aaa Lys | gat Asp | gca Ala 170 | gaa Glu | tat Tyr | gga Gly | ctc Leu | tat Tyr 175 | tcc Ser | 528 |
| atc Ile | tat Tyr | caa Gln | 999 Gly 180 | gga Gly | ata Ile | ttt Phe | gag Glu | ctt Leu 185 | aag Lys | gaa Glu | aat Asn | gac Asp | aga Arg 190 | att Ile | ttt Phe | 576 |
| gtt val | tct Ser | gta Val 195 | aca Thr | aat Asn | gag Glu | cac His | ttg Leu 200 | ata Ile | gac Asp | atg Met | gac Asp | cat His 205 | gaa Glu | gcc Ala | agt Ser | 624 |
| ttt Phe | ttc Phe 210 | ggg GTy | gcc Ala | ttt Phe | tta Leu | gtt Val 215 | ggc Gly | ggt Gly | ggc Gly | ggt Gly | tct Ser 220 | ggt Gly | ggc Gly | ggt Gly | tct Ser | 672 |
| ggt Gly 225 | ggc Gly | ggt Gly | tct Ser | ggt Gly | ggc Gly 230 | gga Gly | tca Ser | acc Thr | tct Ser | gag Glu 235 | gaa Glu | acc Thr | att Ile | tct Ser | aca Thr 240 | 720 |
| gtt val | caa Gln | gaa Glu | aag Lys | caa G1n 245 | caa Gln | aat Asn | att Ile | tct Ser | ccc Pro 250 | cta Leu | gtg Val | aga Arg | gaa G1u | aga Arg 255 | ggt Gly | 768 |
| cct Pro | cag G1n | aga Arg | gta Val 260 | gca Ala | gct Ala | cac His | ata Ile | act Thr 265 | ggg Gly | acc Thr | aga Arg | gga Gly | aga Arg 270 | agc Ser | aac Asn | 816 |
| aca Thr | ttg Leu | tct Ser 275 | tct Ser | cca Pro | aac Asn | tcc Ser | aag Lys 280 | aat Asn | gaa Glu | aag Lys | gct Ala | ctg Leu 285 | ggc Gly | cgc Arg | aaa Lys | 864 |

| | | | | | | | The | raphe | eres | isse | q Li: | stine | ı.tx | t | | |
|--------------------|-------------------|-------------------|-------------------|-----------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|---------------------|---------------------|------|
| ata Ile | aac Asn 290 | tcc Ser | tgg Trp | gaa Glu | tca Ser | tca Ser 295 | agg | agt | ggg | cat | tca | ttc | ctg | agc | aac Asn | 912 |
| ttg Leu 305 | cac His | ttg Leu | agg Arg | aat Asn | ggt Gly 310 | gaa Glu | ctg Leu | gtc Val | atc Ile | cat His 315 | gaa Glu | aaa Lys | ggg Gly | ttt Phe | tac Tyr 320 | 960 |
| tac Tyr | atc Ile | tat Tyr | tcc Ser | caa Gln 325 | aca Thr | tac Tyr | ttt Phe | cga Arg | ttt Phe 330 | cag Gln | gag Glu | gaa Glu | ata Ile | aaa Lys 335 | gaa Glu | 1008 |
| aac Asn | aca Thr | aag Lys | aac Asn 340 | gac Asp | aaa Lys | caa Gln | atg Met | gtc Val 345 | caa Gln | tat Tyr | att Ile | tac Tyr | aaa Lys 350 | tac Tyr | aca Thr | 1056 |
| agt Ser | tat Tyr | cct Pro 355 | gac Asp | cct Pro | ata Ile | ttg Leu | ttg Leu 360 | atg Met | aaa Lys | agt Ser | gct Ala | aga Arg 365 | aat Asn | agt Ser | tgt Cys | 1104 |
| tgg Trp | tct Ser 370 | aaa Lys | gat Asp | gca Ala | gaa Glu | tat Tyr 375 | gga Gly | ctc Leu | tat Tyr | tcc Ser | atc Ile 380 | tat Tyr | caa Gln | 9 9 9 G1y | g g a Gly | 1152 |
| | | | | | | aat Asn | | | | | | | | | | 1200 |
| gag Glu | cac His | ttg Leu | ata Ile | gac Asp 405 | atg Met | gac Asp | cat His | gaa Glu | gcc Ala 410 | agt Ser | ttt Phe | ttc Phe | ggg Gly | gcc Ala 415 | ttt Phe | 1248 |
| tta Leu | gtt val | ggc Gly | ggt Gly 420 | ggc Gly | ggt Gly | tct Ser | ggt Gly | ggc Gly 425 | ggt Gly | tct Ser | ggt Gly | ggc Gly | ggt Gly 430 | tct Ser | g g t Gly | 1296 |
| ggc Gly | gga Gly | tcc Ser 435 | acc Thr | tct Ser | gag Glu | gaa Glu | acc Thr 440 | att Ile | tct Ser | aca Thr | gtt val | caa Gln 445 | gaa Glu | aag Lys | caa Gln | 1344 |
| caa Gln | aat Asn 450 | att Ile | tct Ser | ccc Pro | cta Leu | gtg Val 455 | aga Arg | gaa Glu | aga Arg | ggt Gly | cct Pro 460 | cag Gln | aga Arg | gta Val | gca Ala | 1392 |
| gct Ala 465 | cac His | ata Ile | act Thr | g g g G1y | acc Thr 470 | aga Arg | gga Gly | aga Arg | agc Ser | aac Asn 475 | aca Thr | ttg Leu | tct Ser | tct Ser | cca Pro 480 | 1440 |
| aac Asn | tcc Ser | aag Lys | aat Asn | gaa Glu 485 | aag Lys | gct Ala | ctg Leu | ggc Gly | cgc Arg 490 | aaa Lys | ata Ile | aac Asn | tcc Ser | tgg Trp 495 | gaa Glu | 1488 |
| tca Ser | tca Ser | agg Arg | agt Ser 500 | g g g G l y | cat His | tca Ser | ttc Phe | ctg Leu 505 | agc Ser | aac Asn | ttg Leu | cac His | ttg Leu 510 | agg Arg | aat Asn | 1536 |
| g gt Gly | gaa Glu | ctg Leu 515 | gtc Val | atc Ile | cat His | gaa Glu | aaa Lys 520 | ggg GTy | ttt Phe | tac Tyr | tac Tyr | atc 11e 525 | tat Tyr | tcc S e r | caa Gln | 1584 |
| aca Thr | tac Tyr 530 | ttt Phe | cga Arg | ttt Phe | cag Gln | gag Glu 535 | gaa Glu | ata Ile | | gaa Glu | 540 | aca Thr | aag Lys | aac Asn | gac Asp | 1632 |

Page 21

| | | | | | | | | | | | | | _ | | | |
|--------------------------|-------------------|---------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| aaa Lys 545 | caa Gln | atg Met | gtc Val | caa Gln | tat Tyr 550 | att Ile | tac Tyr | aaa Lys | tac Tyr | aca Thr 555 | agt Ser | tat Tyr | cct Pro | gac Asp | cct Pro 560 | 1680 |
| ata Ile | ttg Leu | ttg Leu | atg Met | aaa Lys 565 | agt Ser | gct Ala | aga Arg | aat Asn | agt Ser 570 | tgt Cys | tgg Trp | tct Ser | aaa Lys | gat Asp 575 | gca Ala | 1728 |
| gaa Glu | tat Tyr | gga G1y | ctc Leu 580 | tat Tyr | tcc Ser | atc Ile | tat Tyr | caa Gln 585 | ggg Gly | gga G1y | ata Ile | ttt Phe | gag Glu 590 | ctt Leu | aag Lys | 1776 |
| gaa Glu | aat Asn | gac Asp 595 | aga Arg | att Ile | ttt Phe | gtt Val | tct Ser 600 | gta Val | aca Thr | aat Asn | gag Glu | cac His 605 | ttg Leu | ata Ile | gac Asp | 1824 |
| atg Met | gac Asp 610 | cat His | gaa Glu | gcc Ala | agt Ser | ttt Phe 615 | ttc Phe | ggg Gly | gcc Ala | ttt Phe | tta Leu 620 | gtt Val | ggc G1y | tga | | 1869 |
| <21 <21 <21 <21 | 1> 2> | 32 522 PRT Arti1 | ficia | al Se | equer | nce | | | | | | | | | | |
| <22 <22 | | escr | ·ipti | ion d | of Ar | ·tif | icia ⁻ | l Sec | quen | :e: : | scTR/ | VIL þ | oept: | ide s | sequence | |
| <40 | 0> | 32 | | | | | | | | | | | | | | |
| Met 1 | Ala | Ile | Ile | Tyr 5 | Leu | Ile | Leu | Leu | Phe 10 | Thr | Ala | val | Arg | Gly 15 | Ala | |
| Ala | Ala | Asp | Tyr 20 | Lys | Asp | Asp | Asp | Asp 25 | Lys | Glu | Phe | Gly | Thr 30 | ser | Glu | |
| Glu | Thr | Ile 35 | Ser | Thr | va1 | Gln | Glu 40 | Lys | Gln | Gln | Asn | 11e 45 | Ser | Pro | Leu | |
| va1 | Arg 50 | Glu | Arg | GТу | Pro | G]n 55 | Arg | val | Аlа | Αla | ніs 60 | Ile | Thr | Gly | Thr | |
| Arg 65 | Gly | Arg | Ser | Asn | Thr 70 | Leu | Ser | Ser | Pro | Asn 75 | Ser | Lys | Asn | Glu | Lys 80 | |
| Аlа | Leu | G1y | Arg | Lys 85 | Ile | Asn | Ser | Trp | Glu 90 | Ser | Ser | Arg | Ser | G]y 95 | ніѕ | |
| Ser | Phe | Leu | Ser 100 | Asn | Leu | His | Leu | Arg 105 | Asn | Gly | Glu | Leu | Val 110 | Ile | нis | |
| Glu | | | | | | | | | | | | | | | | |

Glu Glu Ile Lys Glu Asn Thr Lys Asn Asp Lys Gln Met Val Gln Tyr 130 135 140 Ile Tyr Lys Tyr Thr Ser Tyr Pro Asp Pro Ile Leu Leu Met Lys Ser Ala Arg Asn Ser Cys Trp Ser Lys Asp Ala Glu Tyr Gly Leu Tyr Ser 165 170 175 Ile Tyr Gln Gly Gly Ile Phe Glu Leu Lys Glu Asn Asp Arg Ile Phe $180 \hspace{1.5cm} 185 \hspace{1.5cm} 190$ Val Ser Val Thr Asn Glu His Leu Ile Asp Met Asp His Glu Ala Ser 195 200 205 Phe Phe Gly Ala Phe Leu Val Gly Gly Gly Gly Ser Gly Gly Gly Ser 210 215 220 Gly Gly Gly Ser Gly Gly Ser Thr Ser Glu Glu Thr Ile Ser Thr 225 230 235 240 Val Gln Glu Lys Gln Gln Asn Ile Ser Pro Leu Val Arg Glu Arg Gly 245 250 255 Pro Gln Arg Val Ala Ala His Ile Thr Gly Thr Arg Gly Arg Ser Asn 260 265 270 Thr Leu Ser Ser Pro Asn Ser Lys Asn Glu Lys Ala Leu Gly Arg Lys 275 280 285 Ile Asn Ser Trp Glu Ser Ser Arg Ser Gly His Ser Phe Leu Ser Asn 290 295 300 Leu His Leu Arg Asn Gly Glu Leu Val Ile His Glu Lys Gly Phe Tyr 305 310 315 320 Tyr Ile Tyr Ser Gln Thr Tyr Phe Arg Phe Gln Glu Glu Ile Lys Glu 325 330 335 Asn Thr Lys Asn Asp Lys Gln Met Val Gln Tyr Ile Tyr Lys Tyr Thr 340 345 350 Ser Tyr Pro Asp Pro Ile Leu Leu Met Lys Ser Ala Arg Asn Ser Cys 355 360 365Trp Ser Lys Asp Ala Glu Tyr Gly Leu Tyr Ser Ile Tyr Gln Gly Gly 370 375 380 Page 23

Ile Phe Glu Leu Lys Glu Asn Asp Arg Ile Phe Val Ser Val Thr Asn 385 390 395 400 Glu His Leu Ile Asp Met Asp His Glu Ala Ser Phe Phe Gly Ala Phe 405 410 415 Leu Val Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gln Asn Ile Ser Pro Leu Val Arg Glu Arg Gly Pro Gln Arg Val Ala 450 460 Ala His Ile Thr Gly Thr Arg Gly Arg Ser Asn Thr Leu Ser Ser Pro 465 470 475 480 Asn Ser Lys Asn Glu Lys Ala Leu Gly Arg Lys Ile Asn Ser Trp Glu 485 490 495 Ser Ser Arg Ser Gly His Ser Phe Leu Ser Asn Leu His Leu Arg Asn 500 505 510 Gly Glu Leu Val Ile His Glu Lys Gly Phe Tyr Tyr Ile Tyr Ser Gln 515 520 525 Thr Tyr Phe Arg Phe Gln Glu Glu Ile Lys Glu Asn Thr Lys Asn Asp $530 \hspace{1.5cm} 535 \hspace{1.5cm} 540$ Lys Gln Met Val Gln Tyr Ile Tyr Lys Tyr Thr Ser Tyr Pro Asp Pro $545 \\ 555 \\ 550 $ Ile Leu Leu Met Lys Ser Ala Arg Asn Ser Cys Trp Ser Lys Asp Ala 565 570 575Glu Tyr Gly Leu Tyr Ser Ile Tyr Gln Gly Gly Ile Phe Glu Leu Lys 580 585 590 Glu Asn Asp Arg Ile Phe Val Ser Val Thr Asn Glu His Leu Ile Asp 595 600 605 Met Asp His Glu Ala Ser Phe Phe Gly Ala Phe Leu Val Gly 610 615 620

| <212> DNA <213> Artificial Sequence | |
|--|-----|
| <220> <223> Description of Artificial Sequence: scTNF sequence | |
| <220> <221> CDS <222> (1)(1578) | |
| $^{<\!400>}$ 33 atg gct atc atc ctc atc ctc ctg ttc acc gct gtg cgg ggc gcg Met Ala Ile Ile Tyr Leu Ile Leu Leu Phe Thr Ala Val Arg Gly Ala 1 5 10 | 48 |
| gcc gcg gat tac aaa gac gat gac gat aaa gaa ttc gga tca tct tct Ala Ala Asp Tyr Lys Asp Asp Asp Lys Glu Phe Gly Ser Ser Ser 25 | 96 |
| cga acc ccg agt gac aag cct gta gcc cat gtt gta gca aac cct caa Arg Thr Pro Ser Asp Lys Pro Val Ala His Val Val Ala Asn Pro Gln 45 5 | 144 |
| gct gag ggg cag ctc cag tgg ctg aac cgc cgg gcc aat gcc ctc ctg Ala Glu Gly Gln Leu Gln Trp Leu Asn Arg Arg Ala Asn Ala Leu Leu 50 60 | 192 |
| gcc aat ggc gtg gag ctg aga gat aac cag ctg gtg gtg cca tca gag Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu Val Val Pro Ser Glu 65 | 240 |
| ggc ctg tac ctc atc tac tcc cag gtc ctc ttc aag ggc caa ggc tgc Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu Phe Lys Gly Gln Gly Cys 85 90 95 | 288 |
| ccc tcc acc cat gtg ctc ctc acc cac acc atc agc cgc atc gcc gtc Pro Ser Thn His Val Leu Leu Thr His Thr Ile Ser Arg Ile Ala Val 100 | 336 |
| tcc tac cag acc aag gtc aac ctc ctc tct gcc atc aag agc ccc tgc Ser Tyr Gln Thr Lys Val Asileu Leu Ser Ala Ile Lys Ser Pro Cys 115 125 | 384 |
| cag agg gag acc Cca gag ggg gct gag gcc aag ccc tgg tat gag ccc Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Lys Pro Trp Tyr Glu Pro 130 140 | 432 |
| atc tat ctg gga ggg gtc ttc cag ctg gag aag ggt gac cga ctc agc Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Lys Gly Asp Arg Leu Ser 145 150 155 | 480 |
| gct gag atc aat cgg ccc gac tat ctc gac ttt gcc gag tct ggg cag Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe Ala Glu Ser Gly Gln 165 | 528 |
| gtc tac ttt ggg atc att gcc ctg ggt ggc ggt tct ggt ggc ggt tct Val Tyr Phe Gly Ile Ile Ala Leu Gly Gly Gly Ser Gly Gly Gly Ser 185 | 576 |
| ggt ggc ggt tct ggt ggc gga tca tca tct tct cga acc ccg agt gac Gly Gly Gly Ser Gly Gly Gly Ser Ser Ser Ser Arg Thr Pro Ser Asp Page 25 | 624 |

| aag Lys | cct Pro 210 | gta Val | gcc Ala | cat His | gtt Val | gta Val 215 | gca Ala | aac Asn | cct Pro | caa Gln | gct Ala 220 | gag Glu | ggg Gly | cag Gln | ctc Leu | 672 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|---------------------|---------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| cag G1n 225 | tgg Trp | ctg Leu | aac Asn | cgc Arg | cgg Arg 230 | gcc Ala | aat Asn | gcc Ala | ctc Leu | ctg Leu 235 | gcc Ala | aat Asn | ggc Gly | gtg Val | gag Glu 240 | 720 |
| ctg Leu | aga Arg | gat Asp | aac Asn | cag Gln 245 | ctg Leu | gtg Val | gtg Val | cca Pro | tca Ser 250 | gag Glu | ggc Gly | ctg Leu | tac Tyr | ctc Leu 255 | atc Ile | 768 |
| tac Tyr | tcc Ser | cag Gln | gtc Val 260 | ctc Leu | ttc Phe | aag Lys | ggc Gly | caa Gln 265 | ggc Gly | tgc Cys | ccc Pro | tcc Ser | acc Thr 270 | cat His | gtg Val | 816 |
| ctc Leu | ctc Leu | acc Thr 275 | cac His | acc Thr | atc Ile | agc Ser | cgc Arg 280 | atc Ile | gcc Ala | gtc val | tcc Ser | tac Tyr 285 | cag Gln | acc Thr | aag Lys | 864 |
| | aac Asn 290 | | | | | | | | | | | | | | | 912 |
| gag Glu 305 | ggg Gly | gct Ala | gag Glu | gcc Ala | aag Lys 310 | ccc Pro | tgg Trp | tat Tyr | gag Glu | ccc Pro 315 | atc Ile | tat Tyr | ctg Leu | gga Gly | ggg G1y 320 | 960 |
| gtc val | ttc Phe | cag Gln | ctg Leu | gag Glu 325 | aag Lys | ggt Gly | gac Asp | cga Arg | ctc Leu 330 | agc Ser | gct Ala | gag Glu | atc Ile | aat Asn 335 | cgg Arg | 1008 |
| ccc Pro | gac Asp | tat Tyr | ctc Leu 340 | gac Asp | ttt Phe | gcc Ala | gag Glu | tct Ser 345 | 9 9 9 G1y | cag Gln | gtc val | tac Tyr | ttt Phe 350 | ggg Gly | atc Ile | 1056 |
| att Ile | gcc Ala | ctg Leu 355 | ggt Gly | ggc Gly | ggt Gly | tct Ser | ggt Gly 360 | ggc Gly | ggt Gly | tct Ser | ggt Gly | ggc G1y 365 | ggt Gly | tct Ser | ggt Gly | 1104 |
| ggc Gly | gga Gly 370 | tca Ser | tca Ser | tct Ser | tct Ser | cga Arg 375 | acc Thr | ccg Pro | agt Ser | gac Asp | aag Lys 380 | cct Pro | gta Val | gcc Ala | cat His | 1152 |
| gtt Val 385 | gta val | gca Ala | aac Asn | cct Pro | caa Gln 390 | gct Ala | gag Glu | 9 9 9 G1y | cag Gln | ctc Leu 395 | cag Gln | tgg Trp | ctg Leu | aac Asn | cgc Arg 400 | 1200 |
| cgg Arg | gcc Ala | aat Asn | gcc Ala | ctc Leu 405 | ctg Leu | gcc Ala | aat Asn | ggc Gly | gtg Val 410 | gag Glu | ctg Leu | aga Arg | gat Asp | aac Asn 415 | cag Gln | 1248 |
| ctg Leu | gtg Val | gtg Val | cca Pro 420 | tca Ser | gag Glu | ggc Gly | ctg Leu | tac Tyr 425 | ctc Leu | atc Ile | tac Tyr | tcc Ser | cag Gln 430 | gtc Val | ctc Leu | 1296 |
| ttc Phe | aag Lys | ggc Gly 435 | caa Gln | ggc Gly | tgc Cys | ccc Pro | tcc Ser 440 | acc Thr | cat His | gtg Val | ctc Leu | ctc Leu 445 | acc Thr | cac His | acc Thr | 1344 |
| atc | agc | cgc | atc | gcc | gtc | tcc | tac | cag | | aag age | | aac | ctc | ctc | tct | 1392 |

| Ile | Ser 450 | Arg | Ile | Ala | ٧a٦ | Ser 455 | Tyr | | | | | | Leu | | Ser | |
|---|------------|-------------------|-------------------|---------------------|---------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------|
| gcc Ala 465 | atc Ile | aag Lys | agc Ser | ccc Pro | tgc Cys 470 | cag Gln | agg Arg | gag Glu | acc Thr | cca Pro 475 | gag Glu | ggg Gly | gct Ala | gag Glu | gcc Ala 480 | 1440 |
| aag Lys | ccc Pro | tgg Trp | tat Tyr | gag Glu 485 | ccc P r o | atc Ile | tat Tyr | ctg Leu | gga Gly 490 | 999 G1y | gtc Val | ttc Phe | cag Gln | ctg Leu 495 | gag Glu | 1488 |
| aag Lys | ggt Gly | gac Asp | cga Arg 500 | ctc Leu | agc ser | gct Ala | gag Glu | atc Ile 505 | aat Asn | cgg Arg | ccc Pro | gac Asp | tat Tyr 510 | ctc Leu | gac Asp | 1536 |
| ttt Phe | gcc Ala | gag Glu 515 | tct Ser | 9 9 9 G1y | cag Gln | gtc val | tac Tyr 520 | ttt Phe | ggg G1y | atc Ile | att Ile | gcc Ala 525 | ctg Leu | tga | | 1581 |
| <210> 34 <211> 526 <212> PRT <213> Artificial Sequence | | | | | | | | | | | | | | | | |
| <pre><220> <223> Description of Artificial Sequence: scTNF peptide sequence</pre> | | | | | | | | | | | | | | | | |
| <400 |)> : | 34 | | | | | | | | | | | | | | |
| Met 1 | Ala | Ile | Ile | Tyr 5 | Leu | Ile | Leu | Leu | Phe 10 | Thr | Ala | va1 | Arg | Gly 15 | Ala | |
| Ala | Ala | Asp | Tyr 20 | Lys | Asp | Asp | Asp | Asp 25 | Lys | Glu | Phe | Gly | Ser 30 | Ser | Ser | |
| Arg | Thr | Pro 35 | Ser | Asp | Lys | Pro | va1 40 | Ala | Нis | val | ٧a٦ | Ala 45 | Asn | Pro | Gln | |
| Ala | G1u 50 | Gly | G1n | Leu | G1n | Trp 55 | Leu | Asn | Arg | Arg | Ala 60 | Asn | Ala | Leu | Leu | |
| Ala 65 | Asn | Gly | val | Glu | Leu 70 | Arg | Asp | Asn | Gln | Leu 75 | val | va1 | Pro | Ser | Glu 80 | |
| Gly | Leu | Tyr | Leu | Ile 85 | Tyr | Ser | Gln | val | Leu 90 | Phe | Lys | Gly | Gln | Gly 95 | Cys | |
| Pro | Ser | Thr | His 100 | val | Leu | Leu | Thr | Нis 105 | Thr | Ile | Ser | Arg | Ile 110 | Ala | val | |
| Ser | Tyr | G]n 115 | Thr | Lys | val | Asn | Leu 120 | Leu | Ser | Αla | Ile | Lys 125 | Ser | Pro | Cys | |
| Gln | Arg | Glu | Thr | Pro | Glu | Gly | Αla | Glu | | Lys age | | Trp | Tyr | Glu | Pro | |

Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Lys Gly Asp Arg Leu Ser 145 150 155 160 Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe Ala Glu Ser Gly Gln 165 170 175 Val Tyr Phe Gly Ile Ile Ala Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Ser Ser Ser Arg Thr Pro Ser Asp 195 200 205 Lys Pro Val Ala His Val Val Ala Asn Pro Gln Ala Glu Gly Gln Leu 210 215 220 Gln Trp Leu Asn Arg Arg Ala Asn Ala Leu Leu Ala Asn Gly Val Glu 225 230 235 240 Leu Arg Asp Asn Gln Leu Val Val Pro Ser Glu Gly Leu Tyr Leu Ile 245 250 255 Tyr Ser Gln Val Leu Phe Lys Gly Gln Gly Cys Pro Ser Thr His Val $260 \ \ \, 265 \ \ \, 270$ Leu Leu Thr His Thr Ile Ser Arg Ile Ala Val Ser Tyr Gln Thr Lys 275 280 285 Val Asn Leu Leu Ser Ala Ile Lys Ser Pro Cys Gln Arg Glu Thr Pro 290 295 300 Glu Gly Ala Glu Ala Lys Pro Trp Tyr Glu Pro Ile Tyr Leu Gly Gly 305 310 315 320 Val Phe Gln Leu Glu Lys Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile 340 345 350 Ile Ala Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Ser Gly
355 360 365 Gly Gly Ser Ser Ser Ser Arg Thr Pro Ser Asp Lys Pro Val Ala His 370 380

TherapheresisSeq Listing.txt Val Val Ala Asn Pro Gln Ala Glu Gly Gln Leu Gln Trp Leu Asn Arg 385 390 400 Arg Ala Asn Ala Leu Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln 405 410 415 Leu Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu 420 425 430Phe Lys Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu Thr His Thr 435 440 445 Ile Ser Arg Ile Ala Val Ser Tyr Gln Thr Lys Val Asn Leu Leu Ser 450 455 460 Ala Ile Lys Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala 465 470 475 480 Lys Pro Trp Tyr Glu Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu 485 490 495 Lys Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp 505 510 Phe Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala Leu 515 520 525 <210> 35 2253 <211> <212> DNA <213> Artificial Seguence <220> <223> Description of Artificial Sequence: scFasL-AMAIZe sequence <220> <221> CDS <222> (1)..(2250) <400> 35 atg gac tgg acc tgg cgc gtg ttt tgc ctg ctc gcc gtg gct cct ggg Met Asp Trp Thr Trp Arg Val Phe Cys Leu Leu Ala Val Ala Pro Gly 1 15 48 gcc cac agc cag gta cag ctg gtg cag tct ggg gga ggc atg gta gag Ala His Ser Gln val Gln Leu val Gln Ser Gly Gly Met val Glu 25 96 cct ggg ggg tcc ctt aga ctc tcc tgt gca gcc tct gga ttc act ttc Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe $\frac{3}{40}$ 144

agt aat gcc tgg atg agc tgg gtc cgc cag gct cca ggg aag ggg ctg

192

TherapheresisSeq Listing.txt

Ser Asn Ala Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 60 60 gag tgg gtt ggc cgt ata aaa agc aaa gct ggt ggt ggg aca gca gag Glu Trp Val Gly Arg Ile Lys Ser Lys Ala Gly Gly Gly Thr Ala Glu 65 70 80 240 tac gct gca ccc gtg aaa ggc aga ttc acc atc tca aga gat gat tca Tyr Ala Ala Pro Val Lys Gly Arg Phe Thr Tle Ser Arg Asp Ser Sp Ser $\mathsf{90}$ 288 caa aac acg ctg tat ctg caa atg aac agc ctg aaa acc gac gac aca Gln Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Asp Asp Thr 100 105 1105 336 gcc gtg tat tac tgt acc aca cat gtc tac ggt gcc ccc cgg aac tgg Ala Val Tyr Tyr cys Thr Thr His Val Tyr Gly Ala Pro Arg Asn Trp 115 120 125384 ggc cag gga tcc ctg gtc acc gtc tcc tca gcc tcc acc aag ggc cca Gly Gln Gly Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro 130 135 140 432 aag ctt gaa gaa ggt gaa ttt tca gaa gca cgc gta cag tct gtg ttg Lys Leu Glu Glu Glu Glu Phe Ser Glu Ala Arg Val Gln Ser Val Leu 145 150 160 480 act cag ccg ccc tca gtg tct gcg gcc cca gga cag aag gtc acc atc Thr Gln Pro Ser Val Ser Ala Ala Pro Gly Gln Lys Val Thr Ile 165 170 170 528 tcc tgc tct gga agc agc tcc aac att gga aat aat tat gtc tcc tgg Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Asn Asn Tyr Val Ser Trp 180 185 190 576 tac gtt caa ctc cca gga aca gcc ccc aaa ctc ctc att tat gac aat Tyr Val Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Asp Asn 195 200 2005 624 aat aag cga ttc tca gga gtt cct gac cga ttc tct ggc tcc aag tct Asn Lys Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser 210 2215 220 672 ggc acg tca gcc acc ctg ggc atc acc ggg ctc cag act ggg gac gag Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln Thr Gly Asp Glu 225 240 720 gcc gat tat tac tgc gga gca tgg gat ggc agc ctg cgt gaa gcg gta Ala Asp Tyr Tyr Cys Gly Ala Trp Asp Gly Ser Leu Arg Glu Ala Val 250 255 768 ttc ggc gga ggg acc aag gtc acc gtc cta ggt gcg gcc gca gtt gag Phe Gly Gly Thr Lys Val Thr Val Leu Gly Ala Ala Ala Val Glu 260 265 270 816 ctc gag gcg gcc gcg gat tac aaa gac gat gac gat aaa gaa ttc acg Leu Glu Ala Ala Ala Asp Tyr Lys Asp Asp Asp Lys Glu Phe Thr 280 285 864 cgt gaa aaa aag gag ctg agg aaa gtg gcc cat tta aca ggc aag tcc Arg Glu Lys Lys Glu Leu Arg Lys Val Ala His Leu Thr Gly Lys Ser 290 912

TherapheresisSen Listing tyt

| | TherapheresisSeq Listing.txt | | | | | | | | | | | | | | | |
|-------------------|------------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| aac Asn 305 | tca Ser | agg Arg | tcc Ser | atg Met | cct Pro 310 | ctg Leu | gaa Glu | tgg Trp | gaa Glu | gac Asp 315 | acc Thr | tat Tyr | gga Gly | att Ile | gtc Val 320 | 960 |
| ctg Leu | ctt Leu | tct Ser | gga Gly | gtg Val 325 | aag Lys | tat Tyr | aag Lys | aag Lys | ggt Gly 330 | ggc Gly | ctt Leu | gtg Val | atc Ile | aat Asn 335 | gaa Glu | 1008 |
| act Thr | ggg Gly | ctg Leu | tac Tyr 340 | ttt Phe | gta Val | tat Tyr | tcc Ser | aaa Lys 345 | gta Val | tac Tyr | ttc Phe | cgg Arg | ggt Gly 350 | caa Gln | tct Ser | 1056 |
| tgc Cys | aac Asn | aac Asn 355 | ctg Leu | ccc Pro | ctg Leu | agc ser | cac His 360 | aag Lys | gtc Val | tac Tyr | atg Met | agg Arg 365 | aac Asn | tct Ser | aag Lys | 1104 |
| tat Tyr | ccc Pro 370 | cag Gln | gat Asp | ctg Leu | gtg Val | atg Met 375 | atg Met | gag Glu | ggg Gly | aag Lys | atg Met 380 | atg Met | agc Ser | tac Tyr | tgc Cys | 1152 |
| act Thr 385 | act Thr | ggg Gly | cag Gln | atg Met | tgg Trp 390 | gcc Ala | cgc Arg | agc Ser | agc Ser | tac Tyr 395 | ctg Leu | ggg G1y | gca Ala | gtg Val | ttc Phe 400 | 1200 |
| aat Asn | ctt Leu | acc Thr | agt Ser | gct Ala 405 | gat Asp | cat His | tta Leu | tat Tyr | gtc Val 410 | aac Asn | gta Val | tct Ser | gag Glu | ctc Leu 415 | tct Ser | 1248 |
| ctg Leu | gtc Val | aat Asn | ttt Phe 420 | gag Glu | gaa Glu | tct Ser | cag Gln | acg Thr 425 | ttt Phe | ttc Phe | ggc Gly | tta Leu | tat Tyr 430 | aag Lys | ctc Leu | 1296 |
| ggt Gly | ggc Gly | ggt Gly 435 | tct Ser | ggt Gly | ggc Gly | ggt Gly | tct ser 440 | ggt Gly | ggc Gly | ggt Gly | tct Ser | ggt Gly 445 | ggc Gly | gga Gly | tca Ser | 1344 |
| gaa Glu | aaa Lys 450 | aag Lys | gag Glu | ctg Leu | agg Arg | aaa Lys 455 | gtg Val | gcc Ala | cat His | tta Leu | aca Thr 460 | ggc Gly | aag Lys | tcc Ser | aac Asn | 1392 |
| tca Ser 465 | agg Arg | tcc Ser | atg Met | cct Pro | ctg Leu 470 | gaa Glu | tgg Trp | gaa Glu | gac Asp | acc Thr 475 | tat Tyr | gga Gly | att Ile | gtc Val | ctg Leu 480 | 1440 |
| ctt Leu | tct Ser | gga Gly | gtg Val | aag Lys 485 | tat Tyr | aag Lys | aag Lys | ggt Gly | ggc Gly 490 | ctt Leu | gtg Val | atc Ile | aat Asn | gaa Glu 495 | act Thr | 1488 |
| ggg Gly | ctg Leu | tac Tyr | ttt Phe 500 | gta Val | tat Tyr | tcc Ser | aaa Lys | gta Val 505 | tac Tyr | ttc Phe | cgg Arg | ggt Gly | caa Gln 510 | tct Ser | tgc Cys | 1536 |
| aac Asn | aac Asn | ctg Leu 515 | ccc Pro | ctg Leu | agc Ser | cac His | aag Lys 520 | gtc Val | tac Tyr | atg Met | agg Arg | aac Asn 525 | tct Ser | aag Lys | tat Tyr | 1584 |
| ccc Pro | cag Gln 530 | gat Asp | ctg Leu | gtg Val | atg Met | atg Met 535 | gag Glu | ggg Gly | aag Lys | atg Met | atg Met 540 | agc Ser | tac Tyr | tgc Cys | act Thr | 1632 |
| act Thr 545 | ggg G1y | cag Gln | atg Met | tgg Trp | gcc Ala 550 | cgc Arg | agc Ser | agc Ser | | ctg Leu 555 age | 999 Gly 31 | gca Ala | gtg Val | ttc Phe | aat Asn 560 | 1680 |

| ctt Leu | acc Thr | agt Ser | gct Ala | gat Asp 565 | cat His | tta Leu | tat Tyr | gtc Val | aac Asn 570 | gta Val | tct Ser | gag Glu | ctc Leu | tct Ser 575 | ctg Leu | 1728 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| gtc Val | aat Asn | ttt Phe | gag G1u 580 | gaa Glu | tct Ser | cag Gln | acg Thr | ttt Phe 585 | ttc Phe | ggc Gly | tta Leu | tat Tyr | aag Lys 590 | ctc Leu | ggt Gly | 1776 |
| ggc Gly | ggt Gly | tct Ser 595 | ggt Gly | ggc Gly | ggt Gly | tct Ser | ggt Gly 600 | ggc Gly | ggt Gly | tct Ser | ggt Gly | ggc Gly 605 | gga Gly | tcc Ser | gaa Glu | 1824 |
| aaa Lys | aag Lys 610 | gag Glu | ctg Leu | agg Arg | aaa Lys | gtg val 615 | gcc Ala | cat His | tta Leu | aca Thr | ggc G1y 620 | aag Lys | tcc ser | aac Asn | tca Ser | 1872 |
| agg Arg 625 | tcc Ser | atg Met | cct Pro | ctg Leu | gaa Glu 630 | tgg Trp | gaa Glu | gac Asp | acc Thr | tat Tyr 635 | gga Gly | att Ile | gtc val | ctg Leu | ctt Leu 640 | 1920 |
| tct Ser | gga Gly | gtg val | aag Lys | tat Tyr 645 | aag Lys | aag Lys | ggt Gly | ggc Gly | ctt Leu 650 | gtg Val | atc Ile | aat Asn | gaa Glu | act Thr 655 | ggg Gly | 1968 |
| | | | | | | aaa Lys | | | | | | | | | | 2016 |
| aac Asn | ctg Leu | ccc Pro 675 | ctg Leu | agc Ser | cac His | aag Lys | gtc Val 680 | tac Tyr | atg Met | agg Arg | aac Asn | tct Ser 685 | aag Lys | tat Tyr | ccc Pro | 2064 |
| cag Gln | gat Asp 690 | ctg Leu | gtg Val | atg Met | atg Met | gag G1u 695 | ggg Gly | aag Lys | atg Met | atg Met | agc Ser 700 | tac Tyr | tgc Cys | act Thr | act Thr | 2112 |
| ggg G1y 705 | cag Gln | atg Met | tgg Trp | gcc Ala | cgc Arg 710 | agc Ser | agc Ser | tac Tyr | ctg Leu | ggg Gly 715 | gca Ala | gtg Val | ttc Phe | aat Asn | ctt Leu 720 | 2160 |
| acc Thr | agt Ser | gct Ala | gat Asp | cat His 725 | tta Leu | tat Tyr | gtc Val | aac Asn | gta Val 730 | tct Ser | gag Glu | ctc Leu | tct Ser | ctg Leu 735 | gtc Val | 2208 |
| | | | | | | acg Thr | | | | | | | | tga | | 2253 |

<210> 36 <211> 750 <212> PRT <213> Artificial Sequence

<220> <223> Description of Artificial Sequence: scFasL-AMAIZe peptide sequence <400> 36

Met Asp Trp Thr Trp Arg Val Phe Cys Leu Leu Ala Val Ala Pro Gly $1 \ \ \, 10 \ \ \, 15$

Ala His Ser Gln Val Gln Leu Val Gln Ser Gly Gly Gly Met Val Glu 20 25 30 Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe 35 40 45 Ser Asn Ala Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu 50 55 60 Glu Trp Val Gly Arg Ile Lys Ser Lys Ala Gly Gly Gly Thr Ala Glu 65 70 70 75 80 Tyr Ala Ala Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser 85 90 95 Gln Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Asp Asp Thr 100 105 110 Ala Val Tyr Tyr Cys Thr Thr His Val Tyr Gly Ala Pro Arg Asn Trp 115 120 125 Gly Gln Gly Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro 130 135 140 Lys Leu Glu Glu Gly Glu Phe Ser Glu Ala Arg Val Gln Ser Val Leu 145 150 160 Thr Gln Pro Pro Ser Val Ser Ala Ala Pro Gly Gln Lys Val Thr Ile 165 170 175 Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Asn Asn Tyr Val Ser Trp 180 185 190Tyr Val Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Asp Asn 195 200 205 Asn Lys Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser 210 220 Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln Thr Gly Asp Glu 225 230 235 240 Ala Asp Tyr Tyr Cys Gly Ala Trp Asp Gly Ser Leu Arg Glu Ala Val 245 250 255 Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly Ala Ala Ala Val Glu 260 265 270 Page 33

Leu Glu Ala Ala Ala Asp Tyr Lys Asp Asp Asp Asp Lys Glu Phe Thr 275 280 285 Arg Glu Lys Lys Glu Leu Arg Lys Val Ala His Leu Thr Gly Lys Ser 290 295 300 Asn Ser Arg Ser Met Pro Leu Glu Trp Glu Asp Thr Tyr Gly Ile Val 305 310 315 320 Leu Leu Ser Gly Val Lys Tyr Lys Lys Gly Gly Leu Val Ile Asn Glu 325 330 335 Thr Gly Leu Tyr Phe Val Tyr Ser Lys Val Tyr Phe Arg Gly Gln Ser $340 \ \ \, 345 \ \ \, 350$ Cys Asn Asn Leu Pro Leu Ser His Lys Val Tyr Met Arg Asn Ser Lys 355 360 365 Tyr Pro Gln Asp Leu Val Met Met Glu Gly Lys Met Met Ser Tyr Cys 370 375 380 Thr Thr Gly Gln Met Trp Ala Arg Ser Ser Tyr Leu Gly Ala Val Phe Asn Leu Thr Ser Ala Asp His Leu Tyr Val Asn Val Ser Glu Leu Ser 405 410 415 Leu Val Asn Phe Glu Glu Ser Gln Thr Phe Phe Gly Leu Tyr Lys Leu $420 \hspace{1.5cm} 425 \hspace{1.5cm} 430$ Gly Gly Gly Ser Gly Gly Gly Gly Gly Ser Gly Gly Gly Ser 435 440 445 Ser Arg Ser Met Pro Leu Glu Trp Glu Asp Thr Tyr Gly Ile Val Leu 465 470 480 Leu Ser Gly Val Lys Tyr Lys Lys Gly Gly Leu Val Ile Asn Glu Thr 485 490 495 Gly Leu Tyr Phe Val Tyr Ser Lys Val Tyr Phe Arg Gly Gln Ser Cys $500 \ \ \, 505 \ \ \, 510$ Asn Asn Leu Pro Leu Ser His Lys Val Tyr Met Arg Asn Ser Lys Tyr

Pro Gln Asp Leu Val Met Met Glu Gly Lys Met Met Ser Tyr Cys Thr 530 540 Thr Gly Gln Met Trp Ala Arg Ser Ser Tyr Leu Gly Ala Val Phe Asn 545 550 555 560 Leu Thr Ser Ala Asp His Leu Tyr Val Asn Val Ser Glu Leu Ser Leu 565 570 575 Val Asn Phe Glu Glu Ser Gln Thr Phe Phe Gly Leu Tyr Lys Leu Gly 580 585 590 Gly Gly Ser Gly Gly Ser Gly Gly Gly Ser Gly Gly Ser Glu 595 605 Lys Lys Glu Leu Arg Lys Val Ala His Leu Thr Gly Lys Ser Asn Ser 610 615 620 Arg Ser Met Pro Leu Glu Trp Glu Asp Thr Tyr Gly Ile Val Leu Leu 625 630 635 640 Ser Gly Val Lys Tyr Lys Lys Gly Gly Leu Val Ile Asn Glu Thr Gly
645 650 655 Leu Tyr Phe Val Tyr Ser Lys Val Tyr Phe Arg Gly Gln Ser Cys Asn 660 665 670 Asn Leu Pro Leu Ser His Lys Val Tyr Met Arg Asn Ser Lys Tyr Pro 675 680 685 Gln Asp Leu Val Met Met Glu Gly Lys Met Met Ser Tyr Cys Thr Thr 690 695 700 Gly Gln Met Trp Ala Arg Ser Ser Tyr Leu Gly Ala Val Phe Asn Leu 705 710 715 720 Thr Ser Ala Asp His Leu Tyr Val Asn Val Ser Glu Leu Ser Leu Val 725 730 735 Asn Phe Glu Glu Ser Gln Thr Phe Phe Gly Leu Tyr Lys Leu 740 745 750

<210> 37 <211> 2646

<211> 2646

<213> Artificial Sequence

| <220> <223> Description of Artificial Sequence: scTRAIL-AMAIZe sequence | | | | | | | | | | | | | | | | |
|--|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----|
| <220> <221> CDS <222> (1)(2643) | | | | | | | | | | | | | | | | |
| <400 |)> : | 37 | | | | | | | | | | | | | | |
| atg Met 1 | gac Asp | tgg Trp | acc Thr | tgg Trp 5 | cgc Arg | gtg Val | ttt Phe | tgc Cys | ctg Leu 10 | ctc Leu | gcc Ala | gtg Val | gct Ala | cct Pro 15 | ggg Gly | 48 |
| gcc Ala | cac His | agc Ser | cag G1n 20 | gta Val | cag Gln | ctg Leu | gtg val | cag G1n 25 | tct Ser | ggg Gly | gga Gly | ggc Gly | atg Met 30 | gta Val | gag Glu | 96 |
| cct Pro | ggg Gly | ggg G1y 35 | tcc Ser | ctt Leu | aga Arg | ctc Leu | tcc ser 40 | tgt Cys | gca Ala | gcc Ala | tct Ser | gga Gly 45 | ttc Phe | act Thr | ttc Phe | 144 |
| agt Ser | aat Asn 50 | gcc Ala | tgg Trp | atg Met | agc Ser | tgg Trp 55 | gtc Val | cgc Arg | cag Gln | gct Ala | cca Pro 60 | ggg Gly | aag Lys | ggg Gly | ctg Leu | 192 |
| gag Glu 65 | tgg Trp | gtt val | ggc Gly | cgt Arg | ata Ile 70 | aaa Lys | agc Ser | aaa Lys | gct Ala | ggt Gly 75 | ggt Gly | ggg Gly | aca Thr | gca Ala | gag Glu 80 | 240 |
| tac Tyr | gct Ala | gca Ala | ccc Pro | gtg val 85 | aaa Lys | ggc Gly | aga Arg | ttc Phe | acc Thr 90 | atc Ile | tca Ser | aga Arg | gat Asp | gat Asp 95 | tca Ser | 288 |
| caa Gln | aac Asn | acg Thr | ctg Leu 100 | tat Tyr | ctg Leu | caa Gln | atg Met | aac Asn 105 | agc Ser | ctg Leu | aaa Lys | acc Thr | gac Asp 110 | gac Asp | aca Thr | 336 |
| gcc Ala | gtg va l | tat Tyr 115 | tac Tyr | tgt Cys | acc Thr | aca Thr | cat His 120 | gtc val | tac Tyr | ggt Gly | gcc Ala | ccc Pro 125 | cgg Arg | aac Asn | tgg Trp | 384 |
| ggc Gly | cag Gln 130 | gga Gly | tcc Ser | ctg Leu | gtc Val | acc Thr 135 | gtc val | tcc Ser | tca Ser | gcc Ala | tcc Ser 140 | acc Thr | aag Lys | ggc Gly | cca Pro | 432 |
| aag Lys 145 | ctt Leu | gaa Glu | gaa Glu | ggt Gly | gaa Glu 150 | ttt Phe | tca Ser | gaa Glu | gca Ala | cgc Arg 155 | gta Val | cag Gln | tct Ser | gtg Val | ttg Leu 160 | 480 |
| act Thr | cag Gln | ccg Pro | ccc Pro | tca Ser 165 | gtg Va i | tct Ser | gcg Ala | gcc Ala | cca Pro 170 | gga Gly | cag Gln | aag Lys | gtc Val | acc Thr 175 | atc Ile | 528 |
| tcc Ser | tgc Cys | tct Ser | gga Gly 180 | agc Ser | agc Ser | tcc Ser | aac Asn | att Ile 185 | gga Gly | aat Asn | aat Asn | tat Tyr | gtc Val 190 | tcc Ser | tgg Trp | 576 |
| tac Tyr | gtt Val | caa Gln 195 | ctc Leu | cca Pro | gga Gly | aca Thr | gcc Ala 200 | ccc Pro | Lys | ctc Leu | Leu | att 11e 205 | tat Tyr | gac Asp | aat Asn | 624 |

Page 36

| | | | | | | | | | | | | | • | | | | |
|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|---|------|
| aat Asn | aag Lys 210 | cga Arg | ttc Phe | tca Ser | gga Gly | gtt Val 215 | cct Pro | gac Asp | cga Arg | ttc Phe | tct Ser 220 | ggc Gly | tcc Ser | aag Lys | tct Ser | | 672 |
| ggc Gly 225 | acg Thr | tca Ser | gcc Ala | acc Thr | ctg Leu 230 | ggc Gly | atc Ile | acc Thr | ggg Gly | ctc Leu 235 | cag Gln | act Thr | ggg Gly | gac Asp | gag Glu 240 | | 720 |
| gcc Ala | gat Asp | tat Tyr | tac Tyr | tgc Cys 245 | gga Gly | gca Ala | tgg Trp | gat Asp | ggc Gly 250 | agc Ser | ctg Leu | cgt Arg | gaa Glu | gcg Ala 255 | gta Val | | 768 |
| ttc Phe | ggc Gly | gga Gly | ggg G1y 260 | acc Thr | aag Lys | gtc val | acc Thr | gtc Val 265 | cta Leu | ggt Gly | gcg Ala | gcc Ala | gca Ala 270 | gtt Val | gag Glu | | 816 |
| ctc Leu | gag Glu | gcg Ala 275 | gcc Ala | gcg Ala | gat Asp | tac Tyr | aaa Lys 280 | gac Asp | gat Asp | gac Asp | gat Asp | aaa Lys 285 | gaa Glu | ttc Phe | gga Gly | | 864 |
| | tct Ser 290 | | | | | | | | | | | | | | | | 912 |
| tct Ser 305 | ccc Pro | cta Leu | gtg Val | aga Arg | gaa Glu 310 | aga Arg | ggt Gly | cct Pro | cag Gln | aga Arg 315 | gta Val | gca Ala | gct Ala | cac His | ata Ile 320 | | 960 |
| act Thr | ggg Gly | acc Thr | aga Arg | gga G1y 325 | aga Arg | agc Ser | aac Asn | aca Thr | ttg Leu 330 | tct Ser | tct Ser | cca Pro | aac Asn | tcc Ser 335 | aag Lys | | 1008 |
| | gaa Glu | | | | | | | | | | | | | | | | 1056 |
| agt S er | ggg Gly | cat His 355 | tca Ser | ttc Phe | ctg Leu | agc Ser | aac Asn 360 | ttg Leu | cac His | ttg Leu | agg Arg | aat Asn 365 | ggt Gly | gaa Glu | ctg Leu | | 1104 |
| gtc Val | atc Ile 370 | cat His | gaa Glu | aaa Lys | ggg Gly | ttt Phe 375 | tac Tyr | tac Tyr | atc Ile | tat Tyr | tcc Ser 380 | caa Gln | aca Thr | tac Tyr | ttt Phe | | 1152 |
| cga Arg 385 | ttt Phe | cag Gln | gag Glu | gaa Glu | ata Ile 390 | aaa Lys | gaa Glu | aac Asn | aca Thr | aag Lys 395 | aac Asn | gac Asp | aaa Lys | caa Gln | atg Met 400 | | 1200 |
| gtc Val | caa Gln | tat Tyr | att Ile | tac Tyr 405 | aaa Lys | tac Tyr | aca Thr | agt Ser | tat Tyr 410 | cct Pro | gac Asp | cct Pro | ata Ile | ttg Leu 415 | ttg Leu | | 1248 |
| | aaa Lys | | | | | | | | | | | | | | | 1 | 1296 |
| ctc Leu | tat Tyr | tcc Ser 435 | atc Ile | tat Tyr | caa Gln | ggg Gly | gga Gly 440 | ata Ile | ttt Phe | gag Glu | ctt Leu | aag Lys 445 | gaa Glu | aat Asn | gac Asp | | 1344 |

| | | | | | | | Tho | ranh | oroc | icco | q Li: | ctin | a +v | | | |
|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|------|
| aga Arg | att Ile 450 | ttt Phe | gtt Val | tct Ser | gta Val | aca Thr 455 | aat | gag | cac | ttg | ata | gac | atq | gac | cat His | 1392 |
| gaa Glu 465 | gcc Ala | agt Ser | ttt Phe | ttc Phe | ggg Gly 470 | gcc Ala | ttt Phe | tta Leu | gtt Val | ggc Gly 475 | ggt Gly | ggc Gly | ggt Gly | tct Ser | ggt Gly 480 | 1440 |
| ggc Gly | ggt Gly | tct Ser | ggt Gly | ggc Gly 485 | ggt Gly | tct Ser | ggt Gly | ggc Gly | gga Gly 490 | tca Ser | acc Thr | tct Ser | gag Glu | gaa Glu 495 | acc Thr | 1488 |
| | | | | | | aag Lys | | | | | | | | | | 1536 |
| gaa Glu | aga Arg | ggt Gly 515 | cct Pro | cag Gln | aga Arg | gta Val | gca Ala 520 | gct Ala | cac His | ata Ile | act Thr | ggg G1y 525 | acc Thr | aga Arg | gga Gly | 1584 |
| aga Arg | agc ser 530 | aac Asn | aca Thr | ttg Leu | tct Ser | tct Ser 535 | cca Pro | aac Asn | tcc Ser | aag Lys | aat Asn 540 | gaa Glu | aag Lys | gct Ala | ctg L eu | 1632 |
| ggc Gly 545 | cgc Arg | aaa Lys | ata Ile | aac Asn | tcc Ser 550 | tgg Trp | gaa Glu | tca Ser | tca Ser | agg Arg 555 | agt Ser | ggg Gly | cat His | tca Ser | ttc Phe 560 | 1680 |
| ctg Leu | agc Ser | aac Asn | ttg Leu | cac His 565 | ttg Leu | agg Arg | aat Asn | ggt Gly | gaa Glu 570 | ctg Leu | gtc val | atc Ile | cat His | gaa Glu 575 | aaa Lys | 1728 |
| ggg Gly | ttt Phe | tac Tyr | tac Tyr 580 | atc Ile | tat Tyr | tcc Ser | caa Gln | aca Thr 585 | tac Tyr | ttt Phe | cga Arg | ttt Phe | cag Gln 590 | gag Glu | gaa Glu | 1776 |
| | | | | | | aac Asn | | | | | | | | | | 1824 |
| | | | | | | gac Asp 615 | | | | | | | | | | 1872 |
| aat Asn 625 | agt Ser | tgt Cys | tgg Trp | tct Ser | aaa Lys 630 | gat Asp | gca Ala | gaa Glu | tat Tyr | gga Gly 635 | ctc Leu | tat Tyr | tcc Ser | atc Ile | tat Tyr 640 | 1920 |
| caa Gln | ggg Gly | gga Gly | ata Ile | ttt Phe 645 | gag Glu | ctt Leu | aag Lys | gaa Glu | aat Asn 650 | gac Asp | aga Arg | att Ile | ttt Phe | gtt Val 655 | tct Ser | 1968 |
| gta Val | aca Thr | aat Asn | gag Glu 660 | cac His | ttg L eu | ata Ile | gac Asp | atg Met 665 | gac Asp | cat His | gaa Glu | gcc Ala | agt Ser 670 | ttt Phe | ttc Phe | 2016 |
| ggg Gly | gcc Ala | ttt Phe 675 | tta Leu | gtt Val | ggc Gly | ggt Gly | ggc G1y 680 | ggt Gly | tct Ser | ggt Gly | ggc Gly | ggt Gly 685 | tct Ser | ggt Gly | ggc Gly | 2064 |
| ggt | tct | ggt | ggc | gga | tcc | acc | tct | gag | | acc age | | tct | aca | gtt | caa | 2112 |

| Gly | Ser 690 | Gly | Gly | Gly | Ser | Thr 695 | | | | | 11e 700 | | | | Gln | |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| gaa Glu 705 | aag Lys | caa Gln | caa Gln | aat Asn | att Ile 710 | tct Ser | ccc Pro | cta Leu | gtg Val | aga Arg 715 | gaa Glu | aga Arg | ggt Gly | cct Pro | cag Gln 720 | 2160 |
| aga Arg | gta Val | gca Ala | gct Ala | cac His 725 | ata Ile | act Thr | ggg Gly | acc Thr | aga Arg 730 | gga Gly | aga Arg | agc Ser | aac Asn | aca Thr 735 | ttg Leu | 2208 |
| tct Ser | tct Ser | cca Pro | aac Asn 740 | tcc Ser | aag Lys | aat Asn | gaa Glu | aag Lys 745 | gct Ala | ctg Leu | ggc Gly | cgc Arg | aaa Lys 750 | ata Ile | aac Asn | 2256 |
| tcc Ser | tgg Trp | gaa Glu 755 | tca Ser | tca Ser | agg Arg | agt Ser | ggg G1y 760 | cat His | tca Ser | ttc Phe | ctg Leu | agc Ser 765 | aac Asn | ttg Leu | cac His | 2304 |
| ttg Leu | agg Arg 770 | aat Asn | ggt Gly | gaa Glu | ctg Leu | gtc Val 775 | atc Ile | cat His | gaa Glu | aaa Lys | ggg G1y 780 | ttt Phe | tac Tyr | tac Tyr | atc Ile | 2352 |
| tat Tyr 785 | tcc Ser | caa Gln | aca Thr | tac Tyr | ttt Phe 790 | cga Arg | ttt Phe | cag Gln | gag Glu | gaa Glu 795 | ata Ile | aaa Lys | gaa Glu | aac Asn | aca Thr 800 | 2400 |
| aag Lys | aac Asn | gac Asp | aaa Lys | caa Gln 805 | atg Met | gtc Val | caa G1n | tat Tyr | att Ile 810 | tac Tyr | aaa Lys | tac Tyr | aca Thr | agt Ser 815 | tat Tyr | 2448 |
| cct Pro | gac Asp | cct Pro | ata Ile 820 | ttg Leu | ttg Leu | atg Met | aaa Lys | agt Ser 825 | gct Ala | aga Arg | aat Asn | agt Ser | tgt Cys 830 | tgg Trp | tct Ser | 2496 |
| aaa Lys | gat Asp | gca Ala 835 | gaa Glu | tat Tyr | gga Gly | ctc Leu | tat Tyr 840 | tcc Ser | atc Ile | tat Tyr | caa Gln | ggg G1y 845 | gga Gly | ata Ile | ttt Phe | 2544 |
| gag Glu | ctt Leu 850 | aag Lys | gaa Glu | aat Asn | gac Asp | aga Arg 855 | att Ile | ttt Phe | gtt Val | tct Ser | gta Val 860 | aca Thr | aat Asn | gag Glu | cac His | 2592 |
| ttg Leu 865 | ata Ile | gac Asp | atg Met | gac Asp | cat His 870 | gaa Glu | gcc Ala | agt Ser | ttt Phe | ttc Phe 875 | ggg Gly | gcc Ala | ttt Phe | tta Leu | gtt Val 880 | 2640 |
| ggc G1y | tga | | | | | | | | | | | | | | | 2646 |

<210> 38 <211> 881 <212> PRT <213> Artificial Sequence

<220> <223> Description of Artificial Sequence: scTRAIL-AMAIZe peptide sequence <400> 38

Met Asp Trp Thr Trp Arg Val Phe Cys Leu Leu Ala Val Ala Pro Gly
1 15 Ala His Ser Gln Val Gln Leu Val Gln Ser Gly Gly Gly Met Val Glu 20 25 30 Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe 35 40 45Ser Asn Ala Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu 50 55 60 Glu Trp Val Gly Arg Ile Lys Ser Lys Ala Gly Gly Gly Thr Ala Glu 65 70 80 Tyr Ala Ala Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Gln Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Asp Asp Thr 100 105 110 Ala Val Tyr Tyr Cys Thr Thr His Val Tyr Gly Ala Pro Arg Asn Trp 115 120 125 Gly Gln Gly Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro 130 135 140 Lys Leu Glu Glu Gly Glu Phe Ser Glu Ala Arg Val Gln Ser Val Leu 145 150 155 160 Thr Gln Pro Pro Ser Val Ser Ala Ala Pro Gly Gln Lys Val Thr Ile 165 170 175 Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Asn Asn Tyr Val Ser Trp $180 \hspace{1cm} 185 \hspace{1cm} 185 \hspace{1cm} 190$ Tyr Val Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Asp Asn 195 200 205 Asn Lys Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser 210 215 220 Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln Thr Gly Asp Glu 225 230 235 240 Ala Asp Tyr Tyr Cys Gly Ala Trp Asp Gly Ser Leu Arg Glu Ala Val 245 250 255

Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly Ala Ala Ala Val Glu 260 265 270Leu Glu Ala Ala Ala Asp Tyr Lys Asp Asp Asp Asp Lys Glu Phe Gly 275 280 285 Thr Ser Glu Glu Thr Ile Ser Thr Val Gln Glu Lys Gln Gln Asn Ile 290 295 300 Ser Pro Leu Val Arg Glu Arg Gly Pro Gln Arg Val Ala Ala His Ile 305 310 315 320 Thr Gly Thr Arg Gly Arg Ser Asn Thr Leu Ser Ser Pro Asn Ser Lys 325 330 335 Asn Glu Lys Ala Leu Gly Arg Lys Ile Asn Ser Trp Glu Ser Ser Arg 340 345 350 Ser Gly His Ser Phe Leu Ser Asn Leu His Leu Arg Asn Gly Glu Leu 355 360 365 Val Ile His Glu Lys Gly Phe Tyr Tyr Ile Tyr Ser Gln Thr Tyr Phe 370 380 Arg Phe Gln Glu Glu Ile Lys Glu Asn Thr Lys Asn Asp Lys Gln Met 385 390 395 400 Val Gln Tyr Ile Tyr Lys Tyr Thr Ser Tyr Pro Asp Pro Ile Leu Leu 405 410 415 Met Lys Ser Ala Arg Asn Ser Cys Trp Ser Lys Asp Ala Glu Tyr Gly
420 425 430 Leu Tyr Ser Ile Tyr Gln Gly Gly Ile Phe Glu Leu Lys Glu Asn Asp 435 440 445 Arg Ile Phe Val Ser Val Thr Asn Glu His Leu Ile Asp Met Asp His 450 460 Glu Ala Ser Phe Phe Gly Ala Phe Leu Val Gly Gly Gly Gly Ser Gly 465 470 475 480 Gly Gly Ser Gly Gly Ser Gly Gly Ser Thr Ser Glu Glu Thr 485 490 495 Ile Ser Thr Val Gln Glu Lys Gln Gln Asn Ile Ser Pro Leu Val Arg

Glu Arg Gly Pro Gln Arg Val Ala Ala His Ile Thr Gly Thr Arg Gly 515 520 525 Arg Ser Asn Thr Leu Ser Ser Pro Asn Ser Lys Asn Glu Lys Ala Leu 530 540 Gly Arg Lys Ile Asn Ser Trp Glu Ser Ser Arg Ser Gly His Ser Phe Leu Ser Asn Leu His Leu Arg Asn Gly Glu Leu Val Ile His Glu Lys 565 570 575 Gly Phe Tyr Tyr Ile Tyr Ser Gln Thr Tyr Phe Arg Phe Gln Glu Glu 580 585 590 Ile Lys Glu Asn Thr Lys Asn Asp Lys Gln Met Val Gln Tyr Ile Tyr 595 600 605 Lys Tyr Thr Ser Tyr Pro Asp Pro Ile Leu Leu Met Lys Ser Ala Arg 610 615 620 Asn Ser Cys Trp Ser Lys Asp Ala Glu Tyr Gly Leu Tyr Ser Ile Tyr 625 630 640 Gln Gly Gly Ile Phe Glu Leu Lys Glu Asn Asp Arg Ile Phe Val Ser 645 650 655 Val Thr Asn Glu His Leu Ile Asp Met Asp His Glu Ala Ser Phe Phe 660 665 670 Gly Ala Phe Leu Val Gly Gly Gly Gly Ser Gly Gly Gly Gly 675 680 685 Gly Ser Gly Gly Gly Ser Thr Ser Glu Glu Thr Ile Ser Thr Val Gln 690 695 700 Glu Lys Gln Gln Asn Ile Ser Pro Leu Val Arg Glu Arg Gly Pro Gln 705 710 715 720 Arg Val Ala Ala His Ile Thr Gly Thr Arg Gly Arg Ser Asn Thr Leu 725 730 735 Ser Ser Pro Asn Ser Lys Asn Glu Lys Ala Leu Gly Arg Lys Ile Asn

Ser Trp Glu Ser Ser Arg Ser Gly His Ser Phe Leu Ser Asn Leu His 755 760 765 Leu Arg Asn Gly Glu Leu Val Ile His Glu Lys Gly Phe Tyr Tyr Ile 770 775 780 Tyr Ser Gln Thr Tyr Phe Arg Phe Gln Glu Glu Ile Lys Glu Asn Thr 785 790 795 800 Lys Asn Asp Lys Gln Met Val Gln Tyr Ile Tyr Lys Tyr Thr Ser Tyr 805 810 815 Pro Asp Pro Ile Leu Leu Met Lys Ser Ala Arg Asn Ser Cys Trp Ser 820 825 830 Lys Asp Ala Glu Tyr Gly Leu Tyr Ser Ile Tyr Gln Gly Gly Ile Phe 835 840 845 Glu Leu Lys Glu Asn Asp Arg Ile Phe Val Ser Val Thr Asn Glu His 850 855 860 Leu Ile Asp Met Asp His Glu Ala Ser Phe Phe Gly Ala Phe Leu Val 865 870 875 880 Gly <210> 2358 <211> <212> DNA Artificial Sequence <220> <223> Description of Artificial Sequence: scTNF-AMAIZe sequence <220> <221> CDS <222> (1)..(2355) 48

| agt aat Ser Asn 50 | gcc tgg Ala Trp | atg ag Met Se | tgg r Trp 55 | | rapho cgc Arg | | | | | | | ctg Leu | 192 |
|---------------------------|---------------------------|-------------------------|-----------------------|-------------------|---------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----|
| gag tgg Glu Trp 65 | gtt ggc Val Gly | cgt at Arg Il 70 | a aaa e Lys | agc Ser | aaa Lys | gct Ala | ggt Gly 75 | ggt Gly | ggg Gly | aca Thr | gca Ala | gag Glu 80 | 240 |
| tac gct Tyr Ala | gca ccc Ala Pro | gtg aa Val Ly 85 | a ggc s Gly | aga Arg | ttc Phe | acc Thr 90 | atc Ile | tca Ser | aga Arg | gat Asp | gat Asp 95 | tca Ser | 288 |
| caa aac Gln Asn | | Tyr Le | | | | | | | | | | | 336 |
| gcc gtg Ala val | tat tac Tyr Tyr 115 | tgt ac Cys Th | c aca r Thr | cat His 120 | gtc Val | tac Tyr | ggt Gly | gcc Ala | ccc Pro 125 | cgg Arg | aac Asn | tgg Trp | 384 |
| ggc cag Gly Gln 130 | gga tcc Gly Ser | ctg gt Leu Va | c acc 1 Thr 135 | gtc Val | tcc ser | tca Ser | gcc Ala | tcc Ser 140 | acc Thr | aag Lys | ggc G1y | cca Pro | 432 |
| aag ctt Lys Leu 145 | gaa gaa Glu Glu | ggt ga Gly Gl 15 | u Phe | tca Ser | gaa Glu | gca Ala | cgc Arg 155 | gta Val | cag Gln | tct Ser | gtg Val | ttg Leu 160 | 480 |
| act cag Thr Gln | ccg ccc Pro Pro | tca gt Ser Va 165 | g tct I Ser | gcg Ala | gcc Ala | cca Pro 170 | gga G1y | cag Gln | aag Lys | gtc val | acc Thr 175 | atc Ile | 528 |
| tcc tgc Ser Cys | tct gga Ser Gly 180 | Ser Se | c tcc r Ser | aac Asn | att Ile 185 | gga Gly | aat Asn | aat Asn | tat Tyr | gtc Val 190 | tcc ser | tgg Trp | 576 |
| tac gtt Tyr Val | caa ctc Gln Leu 195 | cca gg Pro Gl | a aca y Thr | gcc Ala 200 | ccc Pro | aaa Lys | ctc Leu | ctc Leu | att Ile 205 | tat Tyr | gac Asp | aat Asn | 624 |
| aat aag Asn Lys 210 | | | | | | | | | | | | | 672 |
| ggc acg Gly Thr 225 | tca gcc Ser Ala | acc ct Thr Le 23 | u Gly | atc Ile | acc Thr | ggg Gly | ctc Leu 235 | cag Gln | act Thr | ggg Gly | gac Asp | gag Glu 240 | 720 |
| gcc gat Ala Asp | tat tac Tyr Tyr | tgc gg Cys G1 245 | a gca y Ala | tgg Trp | gat Asp | ggc G1y 250 | agc Ser | ctg Leu | cgt Arg | gaa Glu | gcg Ala 255 | gta Val | 768 |
| ttc ggc Phe Gly | gga ggg Gly Gly 260 | Thr Ly | g gtc s val | acc Thr | gtc Val 265 | cta Leu | ggt Gly | gcg Ala | gcc Ala | gca Ala 270 | gtt Val | gag Glu | 816 |
| ctc gag Leu Glu | gcg gcc Ala Ala 275 | gcg ga Ala As | t tac p Tyr | aaa Lys 280 | gac Asp | gat Asp | gac Asp | gat Asp | aaa Lys 285 | gaa Glu | ttc Phe | gga Gly | 864 |

tca tct tct cga acc ccg agt gac aag cct gta gcc cat gtt gta gca Ser Ser Ser Arg Thr Pro Ser Asp Lys Pro Val Ala His Val Val Ala 290 295 300 Page 44

912

| aac Asn 305 | cct Pro | caa G1n | gct Ala | gag Glu | ggg Gly 310 | cag Gln | ctc Leu | cag Gln | tgg Trp | ctg Leu 315 | aac Asn | cgc Arg | cgg Arg | gcc Ala | aat Asn 320 | 960 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| gcc Ala | ctc Leu | ctg Leu | gcc Ala | aat Asn 325 | ggc Gly | gtg Val | gag Glu | ctg Leu | aga Arg 330 | gat Asp | aac Asn | cag Gln | ctg Leu | gtg Val 335 | gtg val | 1008 |
| cca Pro | tca Ser | gag Glu | ggc Gly 340 | ctg Leu | tac Tyr | ctc Leu | atc Ile | tac Tyr 345 | tcc Ser | cag Gln | gtc val | ctc Leu | ttc Phe 350 | aag Lys | ggc Gly | 1056 |
| caa Gln | ggc Gly | tgc Cys 355 | ccc Pro | tcc Ser | acc Thr | cat His | gtg Val 360 | ctc Leu | ctc Leu | acc Thr | cac His | acc Thr 365 | atc Ile | agc Ser | cgc Arg | 1104 |
| atc Ile | gcc Ala 370 | gtc Val | tcc Ser | tac Tyr | cag Gln | acc Thr 375 | aag Lys | gtc Val | aac Asn | ctc Leu | ctc Leu 380 | tct Ser | gcc Ala | atc Ile | aag Lys | 1152 |
| | | tgc Cys | | | | | | | | | | | | | | 1200 |
| tat Tyr | gag Glu | ccc Pro | atc Ile | tat Tyr 405 | ctg Leu | gga Gly | ggg Gly | gtc Val | ttc Phe 410 | cag Gln | ctg Leu | gag Glu | aag Lys | ggt Gly 415 | gac Asp | 1248 |
| cga Arg | ctc Leu | agc Ser | gct Ala 420 | gag Glu | atc Ile | aat Asn | cgg Arg | ccc Pro 425 | gac Asp | tat Tyr | ctc Leu | gac Asp | ttt Phe 430 | gcc Ala | gag Glu | 1296 |
| tct Ser | ggg Gly | cag Gln 435 | gtc Val | tac Tyr | ttt Phe | ggg Gly | atc Ile 440 | att Ile | gcc Ala | ctg Leu | ggt Gly | ggc G1y 445 | ggt Gly | tct Ser | ggt Gly | 1344 |
| ggc Gly | ggt Gly 450 | tct Ser | ggt Gly | ggc Gly | ggt Gly | tct Ser 455 | ggt Gly | ggc Gly | gga Gly | tca Ser | tca Ser 460 | tct Ser | tct Ser | cga Arg | acc Thr | 1392 |
| ccg Pro 465 | agt Ser | gac Asp | aag Lys | cct Pro | gta Val 470 | gcc Ala | cat His | gtt Val | gta Val | gca Ala 475 | aac Asn | cct Pro | caa Gln | gct Ala | gag Glu 480 | 1440 |
| ggg Gly | cag Gln | ctc Leu | cag Gln | tgg Trp 485 | ctg Leu | aac Asn | cgc Arg | cgg Arg | gcc Ala 490 | aat Asn | gcc Ala | ctc Leu | ctg Leu | gcc Ala 495 | aat Asn | 1488 |
| ggc Gly | gtg Va l | gag Glu | ctg Leu 500 | aga Arg | gat Asp | aac Asn | cag Gln | ctg Leu 505 | gtg Val | gtg Val | cca Pro | tca Ser | gag Glu 510 | ggc Gly | ctg Leu | 1536 |
| tac Tyr | ctc Leu | atc Ile 515 | tac Tyr | tcc Ser | cag Gln | gtc Val | ctc Leu 520 | ttc Phe | aag Lys | ggc Gly | caa Gln | ggc Gly 525 | tgc Cys | ccc Pro | tcc ser | 1584 |
| acc Thr | cat His 530 | gtg Val | ctc Leu | ctc Leu | acc Thr | cac His 535 | acc Thr | atc Ile | agc Ser | cgc Arg | atc Ile 540 | gcc Ala | gtc Val | tcc Ser | tac Tyr | 1632 |
| cag Gln | acc Thr | aag Lys | gtc Val | aac Asn | ctc Leu | ctc Leu | tct Ser | gcc Ala | Ile | aag Lys age | Ser | ccc Pro | tgc Cys | cag Gln | agg Arg | 1680 |

| 545 5: | Theraph | eresisSeq Listing.txt 555 | 560 |
|---|---|---|------------------------------|
| gag acc cca gag ggg g Glu Thr Pro Glu Gly A 565 | ct gag gcc aag la Glu Ala Lys | ccc tgg tat gag ccc a Pro Trp Tyr Glu Pro I 570 5 | tc tat 1728 le Tyr 75 |
| ctg gga ggg gtc ttc co Leu Gly Gly Val Phe G 580 | ag ctg gag aag In Leu Glu Lys 585 | ggt gac cga ctc agc g Gly Asp Arg Leu Ser A 590 | ct gag 1776 la Glu |
| atc aat cgg ccc gac to Ile Asn Arg Pro Asp T 595 | at ctc gac ttt yr Leu Asp Phe 600 | gcc gag tct ggg cag g Ala Glu Ser Gly Gln V 605 | tc tac 1824 al Tyr |
| ttt ggg atc att gcc c Phe Gly Ile Ile Ala Lo 610 | tg ggt ggc ggt eu Gly Gly Gly 615 | tct ggt ggc ggt tct g Ser Gly Gly Gly Ser G 620 | gt ggc 1872 ly Gly |
| Gly Ser Gly Gly Gly S | ca tca tct tct er Ser Ser Ser 30 | cga acc ccg agt gac a Arg Thr Pro Ser Asp L 635 | ag cct 1920 ys Pro 640 |
| gta gcc cat gtt gta g val Ala His Val Val A 645 | ca aac cct caa la Asn Pro Gln | gct gag ggg cag ctc c Ala Glu Gly Gln Leu G 650 6 | ag tgg 1968 In Trp 55 |
| ctg aac cgc cgg gcc a Leu Asn Arg Arg Ala A 660 | at gcc ctc ctg sn Ala Leu Leu 665 | gcc aat ggc gtg gag c Ala Asn Gly Val Glu L 670 | tg aga 2016 eu Arg |
| gat aac cag ctg gtg g Asp Asn Gln Leu Val V 675 | tg cca tca gag al Pro Ser Glu 680 | ggc ctg tac ctc atc t Gly Leu Tyr Leu Ile T 685 | ac tcc 2064 yr Ser |
| cag gtc ctc ttc aag g Gln Val Leu Phe Lys G 690 | gc caa ggc tgc ly Gln Gly Cys 695 | ccc tcc acc cat gtg c Pro Ser Thr His Val L 700 | tc ctc 2112 eu Leu |
| Thr His Thr Ile Ser A | gc atc gcc gtc rg Ile Ala Val 10 | tcc tac cag acc aag g Ser Tyr Gln Thr Lys V 715 | tc aac 2160 al Asn 720 |
| | | cag agg gag acc cca g Gln Arg Glu Thr Pro G 730 | |
| gct gag gcc aag ccc te Ala Glu Ala Lys Pro Ti 740 | gg tat gag ccc rp Tyr Glu Pro 745 | atc tat ctg gga ggg g Ile Tyr Leu Gly Gly V 750 | tc ttc 2256 al Phe |
| cag ctg gag aag ggt g Gln Leu Glu Lys Gly A 755 | ac cga ctc agc sp Arg Leu Ser 760 | gct gag atc aat cgg c Ala Glu Ile Asn Arg P 765 | cc gac 2304 ro Asp |
| | | gtc tac ttt ggg atc a Val Tyr Phe Gly Ile I 780 | |
| ctg tga Leu 785 | | | 2358 |

<210> 40

<211> 785
<212> PRT
<213> Artificial Sequence <220> <223> Description of Artificial Sequence: TNF-AMAIZe peptide sequence Met Asp Trp Thr Trp Arg Val Phe Cys Leu Leu Ala Val Ala Pro Gly
1 10 15 Ala His Ser Gln Val Gln Leu Val Gln Ser Gly Gly Gly Met Val Glu 20 25 30 Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe 35 40 45 Ser Asn Ala Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu $50 \hspace{1cm} 60$ Glu Trp Val Gly Arg Ile Lys Ser Lys Ala Gly Gly Gly Thr Ala Glu Tyr Ala Ala Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Gln Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Asp Asp Thr 100 105 110 Ala Val Tyr Tyr Cys Thr Thr His Val Tyr Gly Ala Pro Arg Asn Trp Gly Gln Gly Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro 130 135 140 Lys Leu Glu Glu Gly Glu Phe Ser Glu Ala Arg Val Gln Ser Val Leu 145 150 155 160 Thr Gln Pro Pro Ser Val Ser Ala Ala Pro Gly Gln Lys Val Thr Ile 165 170 175 Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Asn Asn Tyr Val Ser Trp 180 185 190 Tyr Val Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Asp Asn 195 200 205 Asn Lys Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser

Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln Thr Gly Asp Glu 225 230 235 240 Ala Asp Tyr Tyr Cys Gly Ala Trp Asp Gly Ser Leu Arg Glu Ala Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly Ala Ala Ala Val Glu 260 265 270 Leu Glu Ala Ala Ala Asp Tyr Lys Asp Asp Asp Asp Lys Glu Phe Gly 275 280 285 Ser Ser Ser Arg Thr Pro Ser Asp Lys Pro Val Ala His Val Val Ala 290 295 300 ASN Pro Gln Ala Glu Gly Gln Leu Gln Trp Leu ASn Arg Arg Ala ASn 305 310 315 320 Ala Leu Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu Val Val 325 330 335 Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu Phe Lys Gly $340 \hspace{1cm} 345 \hspace{1cm} 350$ Gln Gly Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile Ser Arg 355 360Ile Ala Val Ser Tyr Gln Thr Lys Val Asn Leu Leu Ser Ala Ile Lys 370 375 380 Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Lys Pro Trp 385 390 395 400 Tyr Glu Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Lys Gly Asp 405 410 415 Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe Ala Glu 420 425 430 Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala Leu Gly Gly Gly Ser Gly
435 440 445 Gly Gly Ser Gly Gly Gly Ser Gly Gly Ser Ser Ser Ser Arg Thr

TherapheresisSeq Listing.txt
Pro Ser Asp Lys Pro Val Ala His Val Val Ala Asn Pro Gln Ala Glu
465 470 475 480 Gly Gln Leu Gln Trp Leu Asn Arg Arg Ala Asn Ala Leu Leu Ala Asn 485 490 495 Gly Val Glu Leu Arg Asp Asn Gln Leu Val Val Pro Ser Glu Gly Leu
500 505 510 Tyr Leu Ile Tyr Ser Gln Val Leu Phe Lys Gly Gln Gly Cys Pro Ser 515 520 525 Thr His Val Leu Leu Thr His Thr Ile Ser Arg Ile Ala Val Ser Tyr 530 535 540 Gln Thr Lys Val Asn Leu Leu Ser Ala Ile Lys Ser Pro Cys Gln Arg 545 550 555 560 Leu Gly Gly Val Phe Gln Leu Glu Lys Gly Asp Arg Leu Ser Ala Glu 580 585 590 Ile Asn Arg Pro Asp Tyr Leu Asp Phe Ala Glu Ser Gly Gln Val Tyr 595 600 605 Phe Gly Ile Ile Ala Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly 610 615 620Gly Ser Gly Gly Gly Ser Ser Ser Ser Arg Thr Pro Ser Asp Lys Pro 625 630 635 640 Val Ala His Val Val Ala Asn Pro Gln Ala Glu Gly Gln Leu Gln Trp 645 650 655 Leu Asn Arg Arg Ala Asn Ala Leu Leu Ala Asn Gly Val Glu Leu Arg 660 665 Asp Asn Gln Leu Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser 675 680 685

Gln val Leu Phe Lys Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu 690 700 His Thr His Thr Ile Ser Arg Ile Ala Val Ser Tyr Gln Thr Lys Val Asn 705 710 720

Leu Leu Ser Ala Ile Lys Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly 725 730 735

Ala Glu Ala Lys Pro Trp Tyr Glu Pro Ile Tyr Leu Gly Gly Val Phe $740 \hspace{0.5cm} 745 \hspace{0.5cm} 750 \hspace{0.5cm}$

Gln Leu Glu Lys Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp 765 760 765

Tyr Leu Asp Phe Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala 770 780

Leu 785

<210> 41 <211> 4 <212> PRT <213> Artificial Sequence

Description of Artificial Sequence: Peptide linker sequence <400> 41

Gly Gly Gly Ser